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THE USE AND REGULATION OF BIOTECHNOLOGY IN AGRICULTURE

JOINT HEARING

BEFORE THE

COMMITTEE ON AGRICULTURE, NUTRITION, AND FORESTRY

AND THE

SUBCOMMITTEE ON TECHNOLOGY AND THE LAW

OF THE

COMMITTEE ON THE JUDICIARY UNITED STATES SENATE

ONE HUNDREDTH CONGRESS

FIRST SESSION

ON

THE POTENTIAL OF BIOTECHNOLOGY AND AMERICA'S COMPETITIVE POSITION

NOVEMBER 4, 1987

Printed for the use of the Committee on Agriculture, Nutrition, and Forestry and the Committee on the Judiciary

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THE USE AND REGULATION OF BIOTECHNOLOGY IN AGRICULTURE

WEDNESDAY, NOVEMBER 4, 1987

U.S. SENATE,
COMMITTEE ON AGRICULTURE, NUTRITION, AND FORESTRY,
AND
SUBCOMMITTEE ON TECHNOLOGY AND THE LAW OF THE
COMMITTEE ON THE JUDICIARY,
Washington, DC.

The committees met, pursuant to notice, at 10:07 a.m., in room SR-332, Russell Senate Office Building, Hon. Patrick J. Leahy (chairman) presiding.

Present or submitting a statement: Senators Leahy, Harkin, Conrad, McConnell, and Karnes.

STATEMENT OF HON. PATRICK J. LEAHY, A U.S. SENATOR FROM VERMONT

The CHAIRMAN. Good morning. In 13 years in the Senate, I think this is the first time I can recall a joint meeting of the Committee on Agriculture, Nutrition, and Forestry and the Senate Judiciary Committee.

This is a significant hearing that will be directing its attention to many questions that we have raised in both the Agriculture Committee and the Judiciary Committee.

Biotechnology represents a scientific revolution. That revolution could change the complexion of our farm sector. It will create a vast new 21st century marketplace not just for American farm products but for American pharmaceuticals and chemicals as well.

These unprecedented joint hearings will give us all a unique opportunity to address the competitiveness, research, patent and regulatory issues America's burgeoning biotech industry will face over the next two decades.

I convened these hearings because I want to make sure that we analyze those issues thoroughly and with foresight so that we maintain the competitive edge in biotechnology.

At the moment, the United States is winning the biotech race, controlling 84 percent of the industry. But, like semiconductors, Japan and Western European nations may catch up, particularly in the area of product delivery. The key points on the competitiveness of U.S. industry are:

Biotechnology cuts across many market sectors, including agriculture, pharmaceuticals, and chemicals.

Biotechnology is potentially the most significant technological development since computers.

The U.S. invests far more in biotech research than other countries. However, the U.S. lacks a *coordinated* and *long-term* national research program. Our competitors are forming industrial consortia, and encouraging collaborative university, industry, and government projects.

Although the United States will likely remain the world leader in *basic research*, Japan has a better *manufacturing* infrastructure and is likely to capture markets more effectively than the United States.

Biotech competitiveness is not simply the United States and Japan—several European countries and joint European projects are making dramatic progress in biotech research.

The U.S. regulatory environment is no more restrictive than other countries'. However, our regulatory system is more cumbersome and inefficient, with inconsistent and overlapping responsibilities among the U.S. agencies.

Critics of biotechnology point to the further consolidation of the agribusiness industry leading to the demise of the family farm, the dangers of releasing mutant life forms, and the ethical questions of creating life.

It is already clear to me that we must move forward along five parallel paths.

First, we must ensure that America continues to lead the world in biotech research. To do that, we have to set our priorities on basic and applied science. We have to outsmart the Japanese at getting American innovations to markets all over the world.

Second, we must establish international mechanisms that protect biotechnology patents and prevent runaway research.

Third, we must develop a national agenda for biotech research and regulation. Fierce competition in the biotechnology field is already underway. All of our competitors have coordinated national research and regulatory plans. They do not break the backs of their biotech companies with inconsistent, overlapping regulatory requirements. We need to provide good, strong, and efficient regulation for America's biotech companies.

Fourth, we have to develop an extension program that helps the family farmer use this new technology to his or her advantage.

Fifth, we have to begin to explore international mechanisms for the protection of biotech intellectual property and for regulation of biotech products.

I would like to get right to the testimony on this fascinating subject. I welcome our witnesses to this hearing.

Dr. Thomas, who wrote "Lives of a Cell," the book that made biology come alive for millions of American readers is here today. For people like myself, it makes it possible for me to actually understand it. He is here today to help the committees understand the biotechnology revolution and its promise for America.

Dr. Thomas, come on up and join us here. When Senators come in, they can move around you. Dr. Thomas, as we all know, is an eminent biologist and physician. He has served on the faculty of five medical schools; he has been dean of two of them. His presence

here today underscores the importance of our hearing and agribiotechnology.

Doctor, I thank you very, very much for coming. You have already told me that you are willing to stay on through the hearing this morning, and if that can still fit your schedule I would ask you when you finish if you might stay where you are when the other witnesses come forward.

Dr. THOMAS. Yes, indeed.

The CHAIRMAN. Before you begin, Doctor, we have a statement from Senator McConnell which we will put in the record at this point.

[The prepared statements of Senator McConnell and Senator Harkin follow:]

PREPARED STATEMENT OF HON. MITCH MCCONNELL, A U.S. SENATOR FROM KENTUCKY

Mr. Chairman: I want to begin by commending the distinguished Committee Chairman for holding this hearing and, especially, for assembling such an able and distinguished panel to address what I feel is one of the more exciting and important topics this committee must deal with. I certainly look forward to the insights Doctors Thomas and Hardy, and Mr. Harbison have into biotechnology.

Dr. Thomas, in an essay in his book "Lives of a Cell," argued passionately for the need for increased basic research—scientific inquiry often detached from the immediately practical. I think the breakthroughs we have seen in biotechnology are proof of the wisdom of his argument. The ideas which fifteen or twenty years ago were on the drawing boards of laboratories and were probably viewed with skepticism even in the scientific community are now major innovative agricultural technologies being developed for use by farmers in the field. They promise to have as broad an impact on our nation's agriculture as the McCormick Reaper or the cotton gin had on traditional agriculture, or the Green Revolution had on Third World agriculture.

Concomitant with the promise of advance for our farmers come some fundamental questions about what the impact of these advances will have on not only production, but on support industries, and on our farm communities. Additionally, I think it is probably unnecessary to point out the implications for agricultural competitiveness. On another level, we must think carefully about how these technologies will be regulated, and how we will maintain our competitive edge in these technologies over the rest of the world. I look forward to the testimony of today's panel as we take the first steps toward answering these very important questions.

I thank the Chair.

PREPARED OPENING REMARKS OF HON. TOM HARKIN, A U.S. SENATOR FROM IOWA

Mr. Chairman: I congratulate you for holding these hearings which can provide the Committee with considerable insight into the many issues that we face concerning biotechnology: the problems that we must overcome and the horizons that can be opened.

American agriculture faces major difficulties caused by an ability to produce far more than we can sell. We are all aware of the fact that our agricultural "factory", with its level of technology, superior natural resource base, and the amazingly productive American farmer, is incredibly productive. Such a reality is both a blessing and a curse. The blessing, of course, is that we can meet all of our nation's food and fiber needs with ease and at a low cost. The curse results from the fact that we can, and do, over-produce.

With our capacity to produce traditional commodities such as corn or soybeans our farmers face three choices. First, there can be greater and ever greater levels of production in exess of demand creating lower prices that will not cover the costs of production. Second, we can leave part of our capacity idle. Third, we can find new things to do with our capacity, which I believe is the best solution. It is a solution that will take many years to implement. But, biotechnology offers us the possibility to truly accomplish that needed diversity.

We need to expand the use of our agricultural factory beyond the food sector. Starting now, we must develop new plants and varieties of existing crops capable of producing new industrial and commercial products. We need our existing commod-

ities "bio-engineered" so that the range of new products capable of being produced can be expanded many fold.

I am very pleased that the Agriculture Committee reported and the Senate has passed S. 970, the Alternative Agricultural Products Research Act which I introduced. That bill would shift our research priorities toward using the new technologies which are now emerging to expand the types of markets for our agricultural production. The bill also recognizes such an endeavor will require considerable additional basic research and a long period of time. I am hopeful that we can garner strong support from the House as well.

Biotechnology is also crucial as a way to reduce agricultural costs. In a World marketplace, we must keep our relative costs down or we will face further economic difficulties. And, with those lower costs, we will be adding fewer things to the soil that may damage the environment.

The days of simple basic industries with proven technology being successful over the long-term are over. The steel industry and the auto industry make this point all too clear. We need new technology and new knowledge to continue the evolution of our Nation's largest industry—agriculture—so that its full potential can be realized.

But, beyond the need for research funds, beyond the need for a rational mechanism to allocate those funds, we must look at the entire structure of law and our economic stucture to make sure that biotechnololgy research and the applied results of that research can thrive in the United States.

We developed TV. Now I believe, we have only a single TV manufacuturer in the United States.

We led the world in the manufacture of airplanes—and we still do. But, our leadership is in danger of eroding.

We developed the computer. Research at my own alma mater, Iowa State University, played a key part in the development of the computer. But, an ever growing portion of computers are being made overseas.

Biotechnology may become as important in the late 21st century as computers are in this age of information, the silicon age. As a nation, we must make sure that we maintain a level of leadership in this crucial area.

We must ask some basic questions. Are our patent laws structured to provide reasonable protection to reward creativity in this area? Are regulations sufficient to protect our environment and flexible enough to allow research to proceed without undue restraint? Are there sufficient funds available for solid research proposals in both the private sector and in our university and government facilities? Are we providing a structure where scientists in universities and in industry can fully cooperate? Are we making sure that gains in basic research are brought to the attention of those who can apply those gains and bring products to the marketplace? And are those looking at the marketplace talking with those who are making decisions concerning basic research? Lastly, how do our efforts compare with the efforts being undertaken around the World?

Mr. Chairman, I look forward to these important hearings.

The CHAIRMAN. Go ahead, Doctor.

STATEMENT OF LEWIS THOMAS, M.D., PRESIDENT EMERITUS, MEMORIAL SLOAN-KETTERING CANCER CENTER, NEW YORK, NY

Dr. THOMAS. Thank you, Mr. Chairman, and members of the committee. It is a privilege to testify today concerning the present state and future prospects of the biological revolution, and "revolution" is exactly the right word.

I can think of nothing to match the changes that have happened just since the early 1970's. Indeed, never before in this century has the whole field of biological science, including all of medicine, been so spectacularly opened up for new kinds of scrutiny. Terms like "bioengineering" and "gene splicing" have entered everyday conversation. An entire new industry, called biotechnology, has suddenly emerged in the form of small research corporations sprouting in the near vicinity of universities all across the country, doing exciting science all day and all night. The prospects for both basic and applied science are extensive, ranging from new approaches to the diagnosis and treatment of disease in humans, domestic ani-

mals, and plants to such remote enterprises as waste disposal and oil exploration.

The origin of all this was, of course, the discovery of genes and how they are made. This was a long time ago. In 1944, it became known that DNA is the essential substance of the gene, and the Watson-Crick elucidation of the DNA molecule itself came within the next decade. That was basic research at its best, with no notion in anyone's head that the information would one day become greatly useful. Next came the discovery of the language encoded in the DNA molecule, and then in the late 1960's the field simply exploded in what seemed all directions. A set of enzymes was discovered with the extraordinary property of cutting strings of DNA into segments representing individual genes, and it was found that these segments could be isolated, purified, and then inserted into the genetic apparatus of various bacteria, yeasts, and viruses. With these findings, it became possible to clone any individual gene at hand, simply by inducing microbial cells to reproduce that gene, and thus the new technology, and the new prospects for the future, and the new industry.

Already, just a few years along, it has become a feasible enterprise to produce vat-size yields of pure human insulin, pure growth hormone, various factors crucial for the clotting of blood, and any number of natural substances needed for immunologic defense. When certain enzymes are lacking due to genetic defects, it is now theoretically possible to replace them by inserting the appropriate normal genes into the deficient cells, and the whole field of congenital disease will someday be transformed by this technology.

The transfer or improvement of genes for nitrogen fixation in plants is only one example among many of the ways now open to improve existing plant stocks, or to invent totally new strains of plants of agricultural importance, including, notably, the reinforcement of plant resistance to parasitic disease. Within the kingdom of bacteria, it will be possible to invent new forms, with new capacities to degrade waste materials, even the new property of bursting open rock seams for access to petroleum reserves. It does need remembering, however, that bacteria have been doing things of this sort, all on their own, for 3 or more billion years. Recombinant DNA is the most ancient of arts in the kingdom of bacteria, and we are only now beginning to learn how they exchange information and transform each other.

This has been the part of the biological revolution known as the recombinant DNA technology, but it has been associated, as often happens when an explosion occurs in a field of science, with other explosions in other fields at some distance. Cell biology is the term we apply to the whole field, and immunology is becoming the most rapidly expanding enterprise within that field, thanks in part to the recombinant DNA technology. We have learned how antibodies are made by our lymphocytes, and how the genes for designing antibodies are continually being shuffled around within these cells, and we now have lymphocytes that will produce single, absolutely pure antibodies against any antigen we wish and these monoclonal antibodies have become indispensble reagents for research on diseases in general, including such ailments as cancer, Alzheimer's disease, juvenile diabetes, AIDS, and a long list of others.

Most of the work I have been discussing had its beginnings in American university laboratories, and most of the practical applications envisaged for the near-term future will be coming from American biotechnology companies. This is clearly an intellectual advance in pure science for which this country can claim a major share of credit, and, as things stand today, our competitive position in industrial science for the future places us at an advantage. At the same time, however, I must emphasize the importance, and the benefit to us, of the international, or I should say the transnational network of scientific inquiry that exists today.

It is indeed a phenomenon of these days that every issue of our leading scientific journals contains articles coauthored by researchers from this country together with their colleagues in many other centers all around the world. It is the way science works best. At the present time, we Americans are ahead in the game, and I hope we will stay there, but I hope as well that we can maintain and strengthen our intellectual ties to the brightest young scientists in laboratories abroad.

As for the American biotechnology industry, its future—and its competitiveness—will depend, in my view, on how intelligently we arrange the relationships between industry, the universities, and the Government. This, in my view, is the crucial matter at hand. So far, without committees or planning groups or even much in the way of forethought, we have been doing very well. But now, I believe, we should be settling down for a look at the long-term future.

There is an obvious concern for public safety, and it needs to be dealt with openly and continually. There have been all sorts of public worries produced by what has already happened, and surely more to come.

My own view is that of an optimistic but experienced working scientist, and predictably conservative. I have not yet seen or heard of anything to be apprehensive about, nor do I honestly believe that this is a field of science carrying danger for the future. I do not, for instance, believe that ice-minus bacteria are any risk to the environment, and I am all in favor of open experiments designed to restrain the blight of American elm trees. But, I am quick to say, these matters are not for me to decide, for they are public decisions to be made by the public at large and by their representatives. What I would urge is that whenever the inevitable questions about environmental safety do arise, we call in our very best, savviest, and most disinterested scientists as consultants and advisers.

The RAC, recombinant committee of NIH, has developed sensible, workable guidelines for the regulation of recombinant DNA research, and the extension of these rules laid down by this group to industry at large seems to me quite sensible. But there will be new things turning up, new ventures in biomedical science that will seem enchanting to some of us and dangerous to others, and to deal with such problems we need better mechanisms. The Congress' own Office of Technology Assessment is an exceedingly valuable instrument, with a very good record, and I would recommend strengthening the OTA in whatever ways seem appropriate.

For the administration, I would most strongly recommend the reinstitution of the President's Science Advisory Committee, or

PSAC, with a sufficient representation of biomedical science in its membership to cope with the issues to be confronted in the future.

I would also recommend that the White House Office of Science and Technology be restored to its former responsibilities and eminence, and I believe that the National Academy of Sciences and the National Research Council will always be deeply interested in these matters.

I can clearly see, all around the academic circles in which I spend much of my time, encouraging signs of cooperation and interdependence among the basic sciences, as practiced in our major research universities, and the applied biological sciences in industry. Indeed, the lines that used to demarcate these two kinds of research have become so blurred in recent years that I have difficulty telling one from the other. I hope for more of this, more exchange and interchange of graduate students and postdoctoral students back and forth between the university laboratories and their industrial counterparts, more collaborative research, more excitement, and more competition.

I hope that the field will remain wide open for the free exchange of the latest pieces of scientific news and scientific gossip. As a practical matter, confidentiality will be a necessity at times, as it is in all developing industries, but I hope the processes required for patenting and for approval of products by regulatory agencies can be speeded up as much as possible. This is the one area in which we might fall behind other competitors in other countries. Regulation is a necessity, but overregulation will be a severe handicap.

The enterprise will need money, of course. There will be a special need for new and very expensive instruments, since this level of high science is more instrument-dependent than ever before. University laboratories will have to be redesigned and renovated to meet the requirements of the future, and this will be a costly undertaking. The industrial costs for scaling up and production will also be very high. Nevertheless, the investment looks to me like a very sure thing.

There is one special area of basic science needing much more attention than it is receiving at the present time. The broad field of plant genetics is probably the most important, and in some ways the most exciting, of all the new untapped opportunities, and there are many excellent university laboratories ready to embark on fundamental lines of research using plants as their models. The possible payoffs are obvious: new and improved crops, better nutrition for the world's population, better pest control and food preservation, and perhaps most important of all, new insights into plant biology. Many investigators, I am told, are ready to move into the field, but they are uncertain about the sources of funding and the guidelines for doing the new basic science. Whether the Department of Agriculture is to play the leading role here, or whether NIH and NSF should be playing an increasing role in plant research, as I believe they should, are questions needing clarification. The science itself presents immense opportunities.

May I close by repeating myself: The recent advances in biomedical science and technology came as a total surprise to everyone, and they came in large part from basic research carried out for quite different reasons, mainly reasons of plain curiosity about how

nature works. I can make guesses at what practical kinds of things may be turning up in the years just ahead, but I will make no guesses at all for the long-term future. This will depend on how skillfully and imaginatively we maintain and foster our system for encouraging basic research.

No governmental commission, nor any array of academic committees, could possibly have predicted in the 1960's the scientific achievements that are everyday happenings today. The only safe prediction for the decades ahead is that biomedical science is now out in the open, on new high ground, and if we keep our wits about us we are in for one exciting innovation after another, as far ahead as the eye can see.

[The prepared statement of Dr. Thomas, with attachments, follows:]

Statement for Senate Committee on Agriculture, Nutrition and Forestry

November 4, 1987

Lewis Thomas, M.D.*

*President Emeritus, Memorial Sloan-Kettering Cancer Center
Formerly, Professor of Pathology and Medicine, and Dean,
NYU-Bellevue Medical Center
Professor of Pathology and Dean, Yale Medical School, 1969-72
Member, National Academy of Sciences
Member, President's Scientific Advisory Committee, 1968-72
President-Elect, New York Academy of Science, 1988

Mr. Chairman, and members of the Committee, it is a privilege to testify today concerning the present state and future prospects of the biological revolution which is now in its early stages, still gathering momentum, in this country and abroad.

Revolution is indeed the right word. The scientific events that have recently occurred in biology and medicine are quite comparable, in the scale and scope of the transformation they are producing in our understanding of nature, to those more distant events around the turn of the century when physics abruptly changed from the universe of Newton to the strange new world of relativity and quantum mechanics.

I can think of nothing to match the changes that have happened just since the early 1970's. Indeed, never before in this century has the whole field of biological science, including all of medicine, been so spectacularly opened up for new kinds of scrutiny. Terms like "bioengineering" and "gene-splicing" have entered everyday conversation. An entire new industry, called "biotechnology", has suddenly emerged in the form of small research corporations sprouting in the near vicinity of universities all across the country, doing exciting science all day and night. The prospects for both basic and applied science are extensive, ranging from new approaches to the diagnosis and treatment of disease in humans, domestic animals and plants to such remote enterprises as waste disposal and oil exploration. The possible applications in medicine and agriculture alone are simply stunning, and the conceivable benefits from some of the

lines of research now under investigation could not have been imagined, much less planned for, as short a time as 10 years ago.

The origin of all this was, of course, the discovery of genes and how they are made. This was a long time ago. In 1944 it became known that DNA is the essential substance of the gene, and the Watson-Crick elucidation of the DNA molecule itself came within the next decade. This was basic research at its best, with no notion in anyone's head that the information would one day become greatly useful. Next came the discovery of the language encoded in the DNA molecule, and the astonishing simplicity of the mechanism by which the information conveyed by the sequence of bases in DNA is translated into instructions for the assembly of proteins within the cell. Then, in the late 1960's, the field suddenly exploded in what seemed all directions. A set of enzymes was discovered with the extraordinary property of cutting--literally snipping with surgical precision--strings of DNA into segments representing individual genes, and it was found that these segments could be isolated, purified, and then inserted into the genetic apparatus of various bacteria, yeasts and viruses. With these findings, it became possible to clone any individual gene at hand, simply by inducing microbial cells to reproduce that gene--and in some instances the actual products of that gene--in the course of the rapid reproduction of the microbes containing the new gene.

Thus the new technology, and the new prospects for the future, and the new industry. Already, just a few years along,

it has become a feasible enterprise to produce vat-size yield of pure human insulin, pure growth hormone, various factors crucial for the clotting of blood, and any number of natural substances needed for immunologic defense. When certain enzymes are lacking due to genetic defects, it is now theoretically possible to replace them by inserting the appropriate normal genes into the deficient cells, and the whole field of congenital disease will be transformed by this technology.

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rapidly expanding enterprise within that field, thanks in part to the recombinant DNA technology. We have learned how antibodies are made by our lymphocytes, and how the genes for designing antibodies are continually being shuffled around within these cells so that any of millions of foreign substances can be instantly recognized by one or another lymphocyte in the body. We now have lymphocytes that will produce single, absolutely pure antibodies against any antigen we wish, and these monoclonal antibodies have become indispensable reagents for research on diseases in general, including such ailments as cancer, Alzheimer's disease, juvenile diabetes, AIDS, and a long list of others.

Most of the work I've been discussing had its beginnings in American university laboratories, and most of the practical applications envisaged for the near-term future will be coming from American biotechnology companies. This is clearly an intellectual advance in pure science for which this country can claim a major share of credit, and, as things stand today, our competitive position in industrial science for the future places us at an advantage. At the same time, however, I must emphasize the importance, and the benefit to us, of the international, or transnational, network of scientific inquiry. The work going on in laboratories in Princeton, or Stanford, or Harvard, is not only known in intimate detail, as it moves along, to counterpart young scientists in Paris, or Edinburgh, or Gottingen, or Tokyo, it is collaborative work of the kind that used to require

laboratories in the same corridor. It is a phenomenon of these days that in each issue of our leading scientific journals, Science, Nature, Cell, and the like, there are articles coauthored by researchers from all of these places, and many more around the world. It is the way science works best. At the present time, we Americans are ahead in the game, and I hope we will stay there, but I hope as well that we can maintain and strengthen our intellectual ties to the brightest young scientists in laboratories abroad.

As for American biotechnology industry, its future (and its competitiveness) will depend, in my view, on how intelligently we arrange the relationships between industry, the academy, and the government. This, in my view, is the crucial matter at hand. So far, without committees or planning groups or even much in the way of forethought, we have been doing very well. But now, I believe, we should settle down for a look at the long-term future.

There is an obvious concern for public safety, and it needs to be dealt with openly and continually, as far ahead as I can see. There have been all sorts of public worries produced by what has already happened, and surely more to come. How sure can we be that someone, in some crazed scientist's basement, will not let loose a new tiger-bacterium hybrid, ready to do us all in? Will some technician, equipped to manipulate the genes of human beings, decide on his own that two heads are indeed better than one? Or will someone, somewhere, innocently drop something in

the laboratory, endangering the planet? My own view is that of an optimistic but experienced scientist, and predictably conservative. I have not yet seen or heard of anything to be apprehensive about, nor do I honestly believe that this is a field of science carrying danger for the future. I do not believe that ice-minus bacteria are any risk to the environment, and I am all in favor of open experiments designed to restrain the blight of American elm trees. But, I am quick to say, these matters are not for me to decide, for they are public decisions to be made by the public at large, and by their representatives. What I would urge, with as little self-interest as I can shrink to, is that whenever the inevitable questions about environmental safety do arise--as they already have and surely will continue to arise--that we call in our very best, savviest, and most disinterested scientists as consultants and advisors. We are, as a society, not well organized for dealing with such matters of dispute at the present time. The RAC committee of NIH has sensible, workable guidelines for the regulation of recombinant DNA research, and the extension of the rules laid down by this group to industry at large seems to me quite sensible. But there will be new things turning up, new ventures in biomedical science that will seem enchanting to some of us and dangerous to others, and to deal with such problems we need better mechanisms. The Congress's own Office of Technology Assessment is an exceedingly valuable instrument, with a good record, and I would recommend strengthening the OTA in whatever ways seem appropriate. For the

Administration, I would most strongly recommend the reinstitution of PSAC, with a sufficient representation of biomedical science in its membership to cope with the issues to be confronted in the future. And, most of all, I would hope that the White House Office of Science Advisor, with its staff, will be restored to the eminence and influence that it had in the early days of Kistiakowsky and Wiesner, with access this time to sources of wisdom in all the life sciences.

I can clearly see, all around the academic circles in which I spend much of my time, encouraging signs of cooperation and interdependence among the basic sciences, as practiced in our major research universities, and the applied biological sciences in industry. Indeed, the lines that used to demarcate these two kinds of research have become so blurred in recent years that I have difficulty telling one from the other. I hope for more of this, more exchange and interchange of graduate students and postdoctoral students back and forth between the university laboratories and their industrial counterparts, more collaborative research, more excitement, more competition. More fun, in short. I hope that the field will remain wide open for the free exchange of the latest pieces of scientific news. As a practical matter, confidentiality will be a necessity at times, as it is in all developing industries, but I hope the processes required for patenting and for approval of products by regulatory agencies can be speeded up as much as possible. This is the one area in which we might fall behind other competitors in other

countries. Regulation is a necessity, but over-regulation will be a severe handicap.

The enterprise will need money, of course, probably large sums of government and private sector money in the years ahead if it is to become the profitable venture for the country that this country is uniquely qualified to make it. There will be a special need for new and very expensive instruments, since this level of high science is more instrument-dependent than ever before. University laboratories will have to be redesigned and renovated to meet the requirements of the future, and this will be a costly undertaking. The industrial costs for scaling up in production will also be high. Nevertheless, the investment looks to me like a very sure thing.

There is one special area of basic science needing much more attention than it is receiving at the present time. The broad field of plant genetics is probably the most important, and in some ways the most exciting, of all the new opportunities, and there are many excellent university laboratories ready to embark on fundamental lines of research using plants as their models. The possible payoffs are obvious: new and improved crops, better nutrition for the world's population, better pest control and food preservation, and new insights into plant biology. Many investigators are ready to move into the field, but they are uncertain about the sources of funding and the guidelines for doing the new basic science. Whether the Department of Agriculture is to play the leading role here, or whether NIH and

NSF should be playing an increasing part in plant research, are questions needing clarification. The science itself presents immense opportunities.

I close by repeating myself: The recent advances in biomedical science and technology came as a total surprise to everyone, and they came in large part from basic research carried out for quite different reasons, mainly reasons of plain curiosity about how nature works. I can make guesses at what practical kinds of things may be turning up in the years just ahead, but I make no guesses at all for the long-term future. This will depend on how skillfully we maintain and foster our system for encouraging basic research. The new surprises will be coming from the imaginations of our youngest and most talented students, and I hope our system will encourage them to gamble on their brightest guesses. No governmental commission, nor any array of academic committees, could possibly have predicted in the 1960's any of the scientific achievements that are everyday happenings today. The only safe prediction for the decades ahead is that we are now out in the open, on new high ground, and if we keep our wits about us we are in for one exciting innovation after another, as far ahead as the eye can see.

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United States Senate
COMMITTEE ON
AGRICULTURE, NUTRITION, AND FORESTRY
WASHINGTON, DC 20510-6000

November 23, 1987

Lewis Thomas, M.D.
Memorial Sloan-Kettering Cancer Institute
1275 York Avenue
New York, New York 10021

Dear Dr. Thomas,

Thank you for participating in the joint hearing on biotechnology held by the Agriculture Committee and the Judiciary Subcommittee on Technology and the Law.

Enclosed are written questions to which members of the Committees would like you to respond. As I mentioned at the conclusion of the hearing, the questions and answers will be included as part of the permanent hearing record.

Please respond to these questions by December 14, 1987. If you have any questions, please contact Kathleen Merrigan, Senate Agriculture Committee Staff at (202)224-5207 or Marc Rotenberg, Counsel to the Subcommittee at (202)224-3406.

I appreciate all the time you have devoted to this hearing. Please do not worry about providing extensive answers; two or three sentences will suffice.

Again, thank you for your assistance.

Sincerely,

Patrick J. Leahy

PATRICK J. LEAHY
Chairman

QUESTIONS FROM COMMITTEE MEMBERS
FOR DR. LEWIS THOMAS

NOVEMBER 4, 1987 HEARING ON BIOTECHNOLOGY

Questions from Senator Leahy

1. We have the world's premier biomedical research system, anchored by the National Institutes of Health. Should we have a similar national institute dedicated to agricultural research or biotechnology in general?

2. Are there areas of biotechnology that we should decide right now not to pursue? What are the dangers if we do pursue developments in these areas?

3. You described the importance of the transnational network of scientific inquiry. But some would say that these exchanges hurt our country's competitive position. Could you tell us more about the role of the free flow of scientific information and how it affects our economic competitiveness?

4. Does biotechnology present a threat to the biodiversity in the world and if so, how do we lessen the risks?

Questions from Senator Conrad

1. You spoke of the obvious concern for public safety surrounding biotechnological research activities, yet noted that "over-regulation would be a severe handicap" to our emerging biotech industry. In your opinion, are we far enough along in the science of assessing risks to confidently predict environmental impacts? Do we know enough to dispense with some regulatory requirements?

2. You mentioned your hope that we would see in the future more exchange and interchange of graduate students and postdoctoral students between the university laboratories and their industrial counterparts. In your opinion, are we doing enough to encourage young people toward this kind of scientific research? Is the federal government doing enough to facilitate the training of the kind of scientists we will need in the future?

Questions from Senator Karnes

1. What do you consider to be the most productive area of biotechnology up to this point?

2. What do you feel we can learn from other high technology areas which are undergoing rapid development?

Questions from Senator Boschwitz

1. How important are small businesses for biotechnology research and development?

Questions from Senator Harkin

1. What are the barriers to university-company cooperation in biotechnology research that you believe should be modified?

2. What are other countries doing that you believe the United States should adopt to better provide financial resources for their research companies in the area of biotecnnology?

December 14, 1987

Senator Patrick J. Leahy
Chairman
Committee on Agriculture, Nutrition,
and Forestry
Washington, D.C. 20510-6000

Dear Senator Leahy:

I must apologize for lateness in replying to your letter of November 23, which reached me only a few days ago due to a schedule that has had me away from New York.

On the accompanying pages I submit responses to the questions raised by you and your colleagues on the Committee.

May I add that it was a considerable pleasure to meet you on the occasion of the joint hearing? I came away with a feeling of encouragement that men of your intellectual calibre are concerned about the progress of contemporary biomedical science, and with measureably greater confidence that the importance of national science policy is being recognized and dealt with at high levels of government.

With regards, and great respect,

Yours,

Lewis Thomas, M.D.
President Emeritus

LT/sh
enc.

QUESTIONS FROM COMMITTEE MEMBERS
FOR DR. LEWIS THOMAS

NOVEMBER 4, 1987 HEARING ON BIOTECHNOLOGY

Replies to Senator Leahy

1. My impression is that most, if not all of the important and promising problems for the future of agricultural research lie at the most basic level of molecular and structural biology. I am told by some of my younger colleagues now engaged in work at the forefront of biomedical research that they would like nothing better than to begin exploring plant models, where they see opportunities for finding new things about nature beyond the animal cell models now under close scrutiny.

Therefore, in view of the long experience and the remarkable record of achievement by NIH, my recommendation would be to find ways to expand the scope of that institution to include plant research. I would not be in favor of setting up a new Institute for the purpose; several are already engaged in closely related lines of research, and the National Institute of General Medical Science is particularly suited for opening up new zones of basic science.

I have a notion that if word got round that NIH (or NIGMS) was interested in sponsoring fundamental plant research, they would receive any number of exceedingly interesting proposals in the next mail.

2. I am unable to think of any areas of biotechnology that are so potentially hazardous as to preclude research at this time. As has always been true, it is impossible to make long-range predictions about the sorts of technologies that may emerge from truly basic research, but I am reasonably confident that today's biomedical "breakthroughs" are likely to be wholly beneficial in the long run.

My only reservation here, and it has nothing to do with what I am willing to call basic science, would concern attempts to produce permanent alterations in the human germ line. Sooner or later this may become feasible, and I would of course be unalterably opposed.

I would also be opposed to any effort to adapt the new technologies of biomedical research for the purposes of military weaponry. In any case, for as far ahead as I can see, any such efforts would turn out to be feckless and wasteful. Biological warfare has never been a good idea, and trying to improve it by capitalizing on the biological revolution would only make it a worse idea.

3. Concerning the transnational network of scientific inquiry, I cannot imagine how the free and open exchange of basic scientific information can do anything but strengthen the progress of biomedical research in this country. Our brightest, most imaginative and productive young scientists are of course in vigorous competition with their counterparts in other countries, but they are at the same time, and to a much greater degree, dependent on the free flow of information (including scientific gossip) from those laboratories.

I do not really understand how this complex network functions; it is something of a miracle that it does work, and works so well. I believe it has something to do with the irrepresible urge on the part of all good scientists, especially the youngest and brightest ones, to talk about their work and to exchange information. It is part of the fun of doing science, and any change in the system to impose silence or secrecy would simply take away a great part of the fun. And there, not long after, would go the really good science.

4. I do not see a threat to the planet's biodiversity from research in biotechnology. To the contrary, we may be learning more about biological diversity itself and how it works in detail, and what may be happening to it from environmental pollution, and what will surely happen to it from modern warfare.

Replies to Senator Conrad

1. I have great confidence in the RAC committee at NIH, and as I said in my testimony I believe their guidelines are appropriate for the biotechnology industry.

2. The federal government could, and should be doing more to facilitate the exchange of graduate students and post-doctoral students between the country's university and industrial laboratories. There are important and unique things to be learned in each community, and a new sort of fellowship program, highly selective from the outset, would be very useful.

Replies to Senator Karnes

1. The most productive area of biotechnology up to this point has surely been in the obtaining of great masses of totally new and astonishing information. Some of the actual products are beginning to come, many more lie somewhere in the future, but the greatest advances right now are in learning how nature works at very deep levels. The discovery of oncogenes and their role in cancer, the molecular dissection of the complexities in the immune system, the identification and isolation of the chemical signals responsible for the functioning of the brain, and the revelation of the biological details of the various AIDS virus

strains are only a few random examples of the progress already under way.

2. The biologists were joined, 2 or 3 decades back, by some extemely bright physicists who perceived the promise for their skills in modern biology, and these people contributed much to the biological revolution. The biologists would now do well to look back at the history of the transformation from pure physics to high technology as it occurred in the physical sciences, especially in the relationships established between the great research universities and American industry.

Reply to Senator Boschwitz

1. Most of the really exciting events in biotechnology have been taking place in relatively small enterprises, some launched by venture capital, some supported later on by public equity. The flexibility and inclination to take chances in expectation of long-term rewards are more characteristic of small corporations than within the denser bureaucracies of large, established businesses.

Replies to Senator Harkin

1. The principal barriers to university-industry cooperation in biotechnology research have been in matters of confidentiality and secrecy, and the perceived need to withhold publication until patent rights have been secured. Since academic promotion and tenure are dependent on published science, the relationship creates difficulties in the minds of young academic researchers.

Despite this, the system is steadily changing and improving, and I am optimistic that the relationship is working its way along quite rationally.

2. A good many small biotechnology companies are engaged in types of research that most of us would have regarded as pure, basic science a few years back. The only difference is that now certain lines of such research hold the possibility--not the promise, but at least the prospect--of a useful and identifiable product somewhere in the future. The U.S. government, through NIH, NSF and other agencies, should be providing more investigator-initiated grant-in-aid funds for work at this level in more industrial laboratories, especially the smaller ones just starting up.

The CHAIRMAN. Thank you very much, Doctor.

I might note that we have been joined by Senators Conrad and Harkin. Senator Conrad is the chairman of the Subcommittee on Agricultural Research and General Legisiation. That is the subcommittee that has jurisdiction over biotech bills.

Senator Harkin, of course, is the author of S. 970. That is the Harkin-Leahy Alternative Agricultural Products Research Act of 1987 which passed the Senate earlier this year.

I also note in this morning's Wall Street Journal—an article concerning Genentech, Inc., which just won a broad patent covering the basic techniques by which the biotechnology industry turns colonies of microorganisms into factories for the manufacture of useful products. This is a fascinating industry.

[The Wall Street Journal article, "Genentech, Inc. Receives Broad Patent for Basic Gene-Splicing Techniques," can be found on p. 113.]

The CHAIRMAN. Doctor Thomas, you have spent a great deal of time studying this and you have a lot more understanding than we do, but for those of us who are nonscientists we marvel, we wonder about it.

It is hard to imagine just what kind of an impact biotechnology is going to have on our children, on their lives, to say nothing about the lives of ourselves. Can you compare biotechnology to some of the other scientific developments we take for granted?

I do not want to put things in too neat a category, but can this be compared, for example, to the discovery of penicillin?

Dr. THOMAS. Oh, I think it runs considerably beyond the opening up of the field of antibiotics. What really has happened of central importance is not so much that the techniques available in biotechnology will allow us to make new kinds of useful products.

It is the most important tool, the most important technology for exploring nature at a very deep level, exploring life processes, that has ever come into the hands of the biomedical science community.

In a sense, I would, with slight allowances for hyperbole, compare it to what happened at the turn of the century when physics changed from being Newton's physics to being the physics of relativity and the quantum theory. This is the kind of thing that may lie ahead.

We may actually be able to learn in the years ahead how cells work, how tissues work, and sooner or later, I suppose, how at least pieces of the human brain work. It is immensely important. As I said, I have nothing in my long memory in my own professional lifetime that matches the magnitude of this change in our science.

The CHAIRMAN. Thank you, Doctor. You know, in some ways I suppose you could just expand as far as one might in trying to determine just how far we go in this. Take the example of U.S. Government research dollars for space exploration. There are all kinds of spinoffs from the space program, things that we buy as consumer products, microwaves, compact disc players. We certainly got a lot of computer technology out of it.

What kinds of spinoffs might we see in biotechnology if we are spending Government research dollars there?

Dr. THOMAS. I believe that although it seems to many people, and certainly to many of us in medicine and to the public at large, as

though our own field, medicine, has been changed a great deal in the last three decades or so, most of the changes that have actually occurred have been improvements in the way we make diagnoses and the instruments we use for diagnosis and in some limited number of our technologies for treating disease.

During that time, however, most of us have continued to be as bewildered about the mechanisms underlying human disease as we were in my days as a medical student. We have never understood, for instance, what the participants are that are at play in diseases like cancer and Alzheimer's disease and now AIDS, and any number of other human diseases.

The new technology, recombinant DNA, monoclonal antibody, and all the others that will be spinoffs from those, are finally now going to enable us to explore these disease mechanisms in very great depth. And I think that when we have done that, or gotten further than we have, we will be learning ways to turnaround or to reverse or to prevent diseases.

At the same time, I must say, Senator, that it is very hard for me to imagine from here on working on human disease mechanisms without at the same time finding someone down the corridor working on plant pathology who will find whatever turns up in this laboratory of very great interest in that one.

The CHAIRMAN. Well, you say somebody down the corridor. That "down the corridor" might be thousands of miles away and across the ocean. You talked about transnational networks of scientific inquiry in your testimony.

Some have complained that these kinds of exchanges hurt our country's competitive position. Others take obviously a different view. How do you feel about this kind of free flow of scientific information, the transnational flow? Does it enhance our economic competitiveness or does it hurt it?

Dr. THOMAS. I think we would be lost without it. I am not talking now about applied science; I am talking about basic discoveries. These days, it is a commonplace event for a colleague of mine at Sloan-Kettering anywhere in those corridors to open the latest issue of the proceedings of the National Academy of Science or "Cell" or "Science" or "Nature" or one of the other journals and see that a paper has now appeared published from Melbourne or from Edinburgh or from Paris or Tokyo.

He will much of the time simply nod his head and say, oh, yes, that is out, because he already knows what is in the paper. And the network of gossip that is now going on—I can assure you as a former administrator that the telephone bills give you some clue about it.

The CHAIRMAN. I can imagine.

Dr. THOMAS. Everybody knows everything that is going on in Paris and London and New York and Boston and everywhere else I can think of, and it is very healthy.

The CHAIRMAN. I thought just us political junkies did that kind of gossip back and forth, but the scientific community does, too?

Dr. THOMAS. We do it all the time. Our gossip, I think, by and large is more reliable. [Laughter.]

The CHAIRMAN. At least you can prove it empirically.

The National Institutes of Health anchors what some have called the premier biomedical research system. What is there at NIH that could be applied to biotech research in this country? Should we have a national institute dedicated to agricultural biotech or biotech in general? Does that make sense?

Dr. THOMAS. I do not know. Most of us out in the scientific community are apprehensive about expanding the administrative responsibilites at NIH and having them take on more of the kind of bureacratic work that they have had to do and have done so skillfully in the past.

I think much more attention should be paid to plant pathology and plant biology. It could come through the Institute for General Medical Sciences. It could as well become a piece of the responsibility of the other institutes with a commitment to genes and the nature of genes, or it could be a separate institution.

The NIH can do this kind of thing. It is all set up; it has got an admirable, unmatchable system for peer review. Despite all the criticism, it has got a lot of savvy; it knows how to judge good science. I would not hesitate to recommend that the NIH take on more responsibilities for plant biology than it has been able to in the past. NSF could do it as well.

The CHAIRMAN. The reason I ask is I am told the Europeans and Japanese have undertaken a lot of cooperative efforts. Many organizations, such as EMBO, EUREKA, and BRAIN, are being developed by our competitor nations. Do we have those kinds of comparable programs, and can we develop those here in the United States?

Dr. THOMAS. I am sure we can. It depends, really, on what we do to continue to make life exciting to the youngest and brightest of our scientists. I am not talking about people in my generation.

The new people coming into the field, coming in, most of them, in basic biological science, really are very much interested in the problems that exist in plant disease and in plant biology.

They are also interested in what is going on in the biotechnology industry because they have seen—and this is another healthy phenomenon—a lot of very bright people have moved out of the universities and into industry, not so much under the influence of money as under the influence of intellectual opportunities for doing good research in the biotechnology laboratories themselves.

It is a very healthy phenomenon. I do not know how to encourage it, but I would like to see a lot more exchange, as I said, a lot more traffic, intellectual traffic back and forth between the university and the industrial laboratories. It would be a good thing for the country.

The CHAIRMAN. I yield to Senator Conrad and Senator Harkin.

STATEMENT OF HON. KENT CONRAD, A U.S. SENATOR FROM NORTH DAKOTA

Senator CONRAD. Thank you, Mr. Chairman.

There is almost a "Star Trek" quality to what I hear this morning. Referring to political persons as "junkies," maybe we will call

these research people "trekkies." We are off on this search. There is obviously an opportunity side of this and a risk side.

You were talking in your testimony about the need to have a relationship between the academic world, Government, and industry. Specifically, what could we do that would enhance that relationship so that we maximize the opportunity? Do you have any thoughts about what the Federal Government might do to increase the cooperation?

Dr. THOMAS. I am not very good at this, Mr. Conrad. I am not quite sure how to go about it. I know that more opportunities need to be created for young scientists at the postdoctoral level to move into university laboratories doing the kind of basic science that they want to do or to move into industrial laboratories.

There are roadblocks, especially these days with the limitation on funds, for this kind of movement. I would like to see more of it. I would keep an eye out for any signs of increasing requirements for secrecy and confidentiality. This really scares me to death. I hate to think that we could be entering a time when the research going on at the basic level in university laboratories has to be kept undisclosed for periods of time because of some industrial application that might be in the offing. I do not know how to stop that, but it is a dead hand.

Senator CONRAD. Let me ask you a specific question. We have heard a good deal in my subcommittee about there being a tremendous gap in our country between basic research and commercializing that research; that is, that we are quite good at doing basic research, and we are quite good at marketing something once it is commercialized, but we have a problem in comparison to the Japanese and Western Europeans with moving from basic research to the commercialization stage. It has been suggested to us that Government needs to play a greater role in filling that gap; that is, that private industry simply cannot afford to do it and that the Government needs to play a more aggressive role there. What is your notion of that? What is your reaction to that?

Dr. THOMAS. I think we are a lot better off than we were 10 or 15 years ago; certainly than we were in the immediate post-war 1950's. At that time, I remember that there was not only no intellectual connection between the people doing industrial research in my general area of the pharmaceutical industry, for example, and the work going on in the universities.

There was actually a good deal of looking down of noses on both sides. The people who did basic science were regarded as ivory tower types and the people who did applied science were thought of as practical men of the world making more money than they should have been making, and it was not a very congenial atmosphere.

It began to change in the early 1970's when some of the possibilities for expanding basic biological science came, accompanied by new opportunities for application, and now I think it is really working pretty well.

The trouble on the side of industry, I think, is that they have difficulty making investments in really long-term research where the rewards are 10 or 15 years out or may not be coming at all, and something ought to be done about that because especially the small

biotechnology companies are these days a very good environment for doing very good science of this kind that I am not sure whether to call basic or applied because it has got aspects of both, and the Government could do something, I think, about that.

But mostly I would like to see—and as I said, I do not know how to do it, but I would like to see the connection between the scientific community based in the university laboratories and the counterpart community based in industry not only come together, but stay together in the years ahead, and the Government somehow should be able to play a role in this.

Senator CONRAD. We have had proposed to us that there be regional centers that would be Government sponsored that would try to fill in that gap. Does that sound like something that would make sense to you?

Dr. THOMAS. It would depend on what those regional centers were going to do. We already have regional major research universities which need strengthening. I would not like to see the creation of new Max-Planck-like research institutes added to and outside the existing system of universities.

But I would think it might be a good idea to have, here and there, in the country some sort of institutions that were better than we are at random at coordinating the fundamental scientific work going on in the universities and in the industrial laboratories.

Senator CONRAD. Thank you, Mr. Chairman, and Mr. Thomas.

The CHAIRMAN. Thank you. I should also note I may have to step out of here for a few minutes because of a meeting over in the majority leader's office, but the hearing will continue straight on through.

Senator Harkin, I yield to you.

STATEMENT OF HON. TOM HARKIN, A U.S. SENATOR FROM IOWA

Senator HARKIN. Thank you very much, Mr. Chairman. I do have an opening statement I want to make a part of the record, but I will do that later.

[See page 3 for the prepared statement of Senator Harkin.]

The CHAIRMAN. Please feel free to make any part of it now if you would like. I am sorry. I should have yielded to you first for that when you came in.

Senator HARKIN. No; that is fine. I respect other individuals' time, and I appreciate you, Dr. Thomas, coming down here today and testifying. I will just make some comments later on for the record.

I am very interested in the question that Senator Conrad raised about this gap between basic research and actual commercialization. For example, I know of some small companies, some small biotech firms that are engaged in some basic research, but the payoff time is so long, looking down the road, they really cannot raise the kind of venture capital and investments they need for that long-term haul because investors want a little better payoff. Aside from the question of whether or not they will get any payoff at all, it is the length of time involved.

Also, one large business that I know of that has put a lot of money into this, their board is getting a little antsy about it, too.

They are getting a little afraid that they are putting too much into this, and it is costing a lot of money, and they really do not see any payoff.

I guess I would like to perhaps probe you a bit further in your thoughts on the proper role of the Government in both assisting the large concerns that are doing work in this area, and the small ones, that you have said very accurately, are doing some very exciting, new, innovative things out there, but I am afraid a lot of them are going to die on the vine for lack of funds—and this is very capital-intensive. Research costs a lot of money.

The Government's role so far has been mainly one of regulation. We are talking about protecting the public from certain harmful strains entering the domestic field, things like that.

I wonder if there is not a different role for the Government to play in financing, being supportive, in terms of some capital assistance, long-term patent rights—that kind of thing—that would protect these people for a long time down the road.

Again, I just wonder if you have any further thoughts on that?

Dr. THOMAS. I agree, and perhaps I should have carried further the remarks I have in my prepared statement along this line. Certainly, in the last several weeks, the small biotechnology companies are agitated about whether they are going to keep on doing the kind of science that they need to do, in the number of years that they need, before they can come to the marketplace.

I agree with you, that the large companies are also beginning to worry about the investments that they are making, and that we, in the universities, expect them to keep making in basic science in university laboratories.

I think there is a role, an important role for the Government in this, and part of that role is to provide stability for long term—I mean 10 to 15 years research, where sensible scientists are justified in having an informed hunch that something good is likely to come out, without making policies, but likely to come out at the end, and there are lots of opportunities like this.

I think this would be new for this country, because it would mean making some kind of grant mechanism available to industry. Certainly, changing our patent constraints would have an effect on the amount of money that the large companies would be willing to put in.

But I would have no objection, and I know that it is now a possibility to have a grant-in-aid mechanisms for fundamental research, or for this mix of fundamental and implied research going out to the industrial laboratories, and especially the small ones that are now so interesting, and just starting up.

Senator HARKIN. Dr. Thomas, in my former life in the House, I served on the Science and Technology Committee, and at that time chaired a Subcommittee on Aviation and Materials.

I think, perhaps, there might be a model that we have done in the past. Through NASA, we put a lot of taxpayers' money into the development of new materials, and indeed, new engines for airplanes that were adopted by the private industry, and, in return, they have paid us back.

There was a provision put in there that there would be funding, and then there would be a payback later on. If they used it, and if

they made money on it, then they paid the Government back, and that is now in the process of happening right now. And we have the new quiet engines, and much more fuel-efficient engines that airplanes use, and that money is going back in to NASA.

So maybe there is something there, in that kind of a technology investment that we have made in the past, which I think has helped us out.

Sort of along those lines, on a scale of 1 to 10, 10 being the most important, how important is it for us at the Federal level to invest heavily into mapping the human genome?

I have heard that it is going to take $3 billion. I have heard $4 billion. How important is that?

Dr. THOMAS. I have to go carefully, because no matter what I say, I am going to make new enemies.

Senator HARKIN. Do you want me to rephrase the question? [Laughter.]

Dr. THOMAS. Sooner or later the genome is going to be mapped, and it is going to be sequenced, the whole thing. If we take no steps right now, if we do not try to make it into a "moon landing," it is going to happen anyway as the technology for sequencing gets better and gets cheaper, and my preference is to wait until that time comes.

I do not really see—but this may be my ignorance working against me—anything urgent about knowing the sequence of an entire human genome, particularly since I do not know who that human is going to be, or how different he is going to be from another human, and most particularly, because I am aware of something between 5 and 10 percent of the DNA in the human genome, that any of us know about what it is up to.

But at some point in the 1990's, or at the turn of the century, we will have technologies that can sequence the whole genome. I would not put megabucks into it at the present time, but I must tell you—as you undoubtedly know—that there are some extremely eminent scientists in the country who feel just the opposite.

Senator HARKIN. I know. I have talked to them, I think——

Dr. THOMAS. They have talked to you.

Senator HARKIN. Yes, they have talked to me. That is why I was interested in your comments on it. I see what you mean by "making some enemies."

Dr. THOMAS. My enthusiasm for this venture would have to rise to be considered flagging. [Laughter.]

Senator HARKIN. Well, that is interesting.

The CHAIRMAN. That is language we Vermonters can understand.

Senator HARKIN. I thought we have to move ahead very expeditiously on this. I will have to think about that now, and investigate that a little bit further.

I guess we have the ability to begin that process right now?

Dr. THOMAS. It is already going on, but it is not going on in a highly coordinated fashion. But sequences are being worked out here and there. Mapping is already going on. A lot of work is revealing parts of the genome, and the only question is: When do you want to know the entire sequence?

Senator HARKIN. The whole thing. Well, as has been presented to me, that we really will not be able to do much of the work that we want to do unless we know the thing. You can know bits and pieces, but how they correlate to other bits and pieces is most important. Well, I will just have to look at that because I thought it was most important that we move ahead on that.

So, on a scale of 1 to 10, you are way down there, right?

Dr. THOMAS. I am way down. But I have got other things on top.

Senator HARKIN. Well, let me ask you this, then.

The CHAIRMAN. If the Senator would yield just a moment.

I want to go to the meeting in Senator Byrd's office, and in a few minutes I am going to turn it over to you, Tom. But I asked Dr. Thomas earlier, before the hearing started, when we bring up the next panel, Mr. Harbison and Dr. Hardy, if he might stay up here with us, and he is willing to do it.

Because one of the questions I will ask, then, of the three of them, after Mr. Harbison and Dr. Hardy have had a chance to testify, will be: What do we have to fear from the release of biotech products into our environment? Are there areas of biotechnology we should decide today not to pursue—the sort of "Frankenstein factor"? I am going to come back and ask the question, but just so that everybody will have it kind of in mind, and I will be back to you in a few minutes, and welcome Senator Karnes who has joined us here, too.

Senator HARKIN. Do you want me to just——

The CHAIRMAN. It is all yours.

Senator HARKIN [presiding]. Well, obviously, this committee does not have much jurisdiction over the mapping of the human genome, but I do have a great interest in mapping out other things like soybeans and corn. I do not know whether you want to address yourself to that, or not.

Dr. THOMAS. I agree with that.

Senator HARKIN. You would think we should move a little bit faster in that area?

Dr. THOMAS. Yes.

Senator HARKIN. Well, now, I am interested. Tell me why.

Dr. THOMAS. Well, I think it is simpler, and I think there is more likely to be information, totally new information emerging from it.

The systems are easier to manipulate, experimentally, than the human system is, and I think there are very real possibilities for scientific advance if we can get information about the total sequence of plants, individual plants, and individual experiment or laboratory animals.

I am just not as bullish about the information, or the usefulness of the information that we are going to get from knowing the human genome at the present time, until we learn a lot more than we do know about the actual mechanisms of human disease.

Senator HARKIN. Thank you very much, Dr. Thomas.

Senator Karnes.

STATEMENT OF HON. DAVID K. KARNES, A U.S. SENATOR FROM NEBRASKA

Senator KARNES. Mr. Chairman, I have a statement for the record. If I could have unanimous consent I would so submit it, and I have some questions that I would like to submit to the panelists afterward.

Unfortunately, I have a Banking Committee hearing at 11, and I am going to have to run out. But I hope to be back to hear some of the discussion on this fascinating topic. I am glad to see that you are interested in spending a bit more time, at least on your level of priorities, as far as agronomic research. I think that could produce some great benefits, and I think, as you very well state, it may be a bit simpler, at least from an ethical point of view, to deal with some of those things maybe right now. Maybe not.

But if that would be appropriate, Mr. Chairman, I do have my statement, and then I will excuse myself, and I hope to return shortly.

Senator HARKIN. Thank you very much, Senator Karnes. Without objection your statement will be printed in the record in its entirety.

[The prepared statement of Senator Karnes follows:]

PREPARED STATEMENT OF HON. DAVID K. KARNES, A U.S. SENATOR FROM NEBRASKA

I would like to thank our distinguished guests for coming here today to discuss the potential of biotechnology. As we all know, biotechnology is an emerging science which poses great opportunities for those nations and industries that are able to finance and carry through on the research and development of this vital area.

At this time, the United States is at the forefront of biotechnology as we have been a leader in many areas of research. However, biotechnology is still a young science and no country is very far ahead of the others. Many countries realize that the stakes are high and have put large resources behind the development of this science. The Netherlands, West Germany, Belgium and Japan are all devoting considerable attention to the development of biotechnology research. That countries which are not known for their high technology are involved in this work should tell us that we must continue to assign this a high priority. Failure to do so would show that we are not committed to maintaining our position as the pre-eminent world power in research and in agriculture.

So far, America's land-grant universities have been some of the most productive in the amount of research and accomplishments on the subject of biotechnology. They must receive most of the credit up to this point in ensuring that the United States is pre-eminent in the research of biotechnology. One of the most influential of these land-grant universities continues to be the University of Nebraska at Lincoln. Nebraska has long recognized the importance of technology in the future of agriculture and biotechnology is another form of advancing agriculture that the University of Nebraska has focused some of its best minds on.

There are several reasons why universities such as Nebraska have done so well. For instance, academia and industry used to be far apart in terms of what each felt should be the ultimate goal of research and funding. In the last couple of decades, however, business, government and academia have come together on common ground on basic research. Grants from the industrial sector have never been more abundant. Industry is now allowing universities to basic research which does not have any immediate application. Universities are following through with their research and are looking toward how their research can benefit mankind.

Until recently, almost all research in the area of agriculture was geared toward increasing yields on our available land to meet a growing world demand. With large grain surpluses, our focus has turned to making our agricultural industry into a more efficient, lower cost producer of those products that we already have a comparative advantage in. Experimentation is also occurring in the area of alternative uses for products. From this, we have already developed plastics which utilize corn starch and which decompose naturally in a few years.

In Lincoln, work has already begun on "designer crops" that will closely conform to the intended use of the crop. For instance, in the near future, if a new type of corn is needed that is higher in oil to make corn oil-based products, we will have the technology to develop a new strain of corn with that characteristic. Other projects being worked on include new methods for manufacturing animal vaccines using biotechnological practices. Researchers at Lincoln are also developing new ways of transferring genes between unlike species of plants. This will allow us to more conveniently move desirable characteristic from one plant type to another. This transfer, called combined tissue culture, will occur in one generation instead of over several. The University of Nebraska is considered a pioneer in this area.

One of the problems we are facing now is that some universities and areas of the country are benefiting from this trend of increased funding more than others. By narrowing the scope of institutions which receive funds, we potentially shut out schools, students and researchers from being able to contribute to this new revolution. Our land-grant colleges, such as the University of Nebraska-Lincoln, are well situated to provide, as they have been, leadership in biotechnology. It would be a shame for those universities which do not have wide ranging name recognition to miss out on important advances if it is only because money was not allocated well.

We must also encourage the use of this basic research toward practical ends. That means we must go beyond having the ability to make a product to being able to produce it at the best possible price so that we may be a world leader. This is one area where the United States has been deficient in the recent past.

This should not necessarily mean that we must imitate the Japanese model of heavy government involvement in all phases of basic research and development of products. While this method deserves to be studied, it is not necessarily the best system available or what is best for the United States. We must hold forums such as this to determine what the proper relationship of government, business and academia are.

Senator HARKIN. Why don't we move ahead right now. Could we have the next panel come up, and I wonder, Dr. Thomas, if you could just stay here with us and be a part of that panel.

We will call Mr. Earle Harbison, Jr., president and chief operating officer of the Monsanto Co., and Dr. Ralph Hardy, president of Boyce Thompson Institute, Cornell University, and deputy chairman of BioTechnica International, Inc. of Cambridge, Massachusetts.

Mr. Harbison will discuss America's competitive position and highlight biotechnology activities around the world, including patenting, regulatory, and other impediments to American success in biotechnology which we have just raised here.

Dr. Hardy, as I said, is president of Boyce Thompson Institute for plant research at Cornell University. He sits on the executive committee of the National Research Council's Board on Agriculture, and the International Committee on Genetic Experimentation.

From 1979 to 1984, Dr. Hardy served as Director of Life Sciences at Du Pont.

Again, we want to welcome both of you gentlemen to the committee. Thank you for taking your valuable time to be here and to give us your thoughts on this most important subject. I would just recognize Mr. Harbison first, in the order that I have them in front of me.

Again, thank you for being here. Your prepared statement will be made a part of the record in its entirety, and I would just ask you to proceed as you so wish, and to highlight it as you want to.

STATEMENT OF EARLE H. HARBISON, JR., PRESIDENT AND CHIEF OPERATING OFFICER, MONSANTO CO., ST. LOUIS, MO

Mr. HARBISON. Thank you very much, Mr. Chairman. I am delighted to be here both as a representative of Monsanto and also as

an advocate for biotechnology, and I will try and summarize my comments briefly for you.

Dr. Thomas has covered the invention, the creation, if you will, of biotechnology some 15 years ago, and, it has, indeed, in our opinion, brought us to the brink of a new industrial revolution. I would certainly echo his remarks. I do not think I have to dwell on that with the members of this committee.

The contributions biotechnology can make to human health are by now obvious. For example, tissue plasminogen activator (tPA) in relieving heart attacks, human growth hormone, and human insulin. Senator Leahy spoke to that this morning. The human growth hormone that you addressed, Dr. Thomas. Human insulin. Dozens of new diagnostic tools being brought to the market, new therapies to treat disease. AIDS, malaria, all the rest of the issues we have talked about.

Treatments that cannot be reached with the traditional tools of medicine. And agriculture, which is this committee's jurisdiction, and one of Monsanto's main areas of research, we believe that biotechnology offers the most exciting and dramatic prospect for improving the reliability and efficiency of farming literally since man began tilling soil.

The ability to provide the world's crops with added protection from insects, from disease, and stresses, is rapidly being demonstrated today. Nature offers us a huge menu of beneficial traits developed literally through millions of years of evolution, and we now know how to transfer some of those traits across species lines, and we will expand this knowledge greatly in the future.

We can do it rapidly, we can do it precisely, and we believe with great predictability of results, as opposed to the random and time-consuming process of traditional plant breeding.

We think the results are going to be an enormous increase in the efficiency and productivity of farming, and a substantial competitive edge for the country, whose farmers are first to receive the new products.

With your indulgence, if I may, Senator, I would like to show you some examples of what I mean drawn from our own work. I am no scientist, but I do not think it takes a scientist to see some of these results that I want to show you.

Last June, in a test field in southern Illinois, after receiving approval from the Department of Agriculture, we planted three genetically altered types of tomato seedlings. The field was harvested in October, and the data are being compiled now, but this photograph was taken in our labs, and I think it speaks for itself.

[See page 76 for the photograph of the tomato seedlings.]

Mr. HARBISON. The tomato plant on the right was stripped almost bare by caterpillars, specifically, the tobacco hornworm which—to those of you who know it—is a large, homely, and ravenous caterpillar familiar to any backyard gardener who has tried to raise tomatoes. The plant on the left was attacked by the same pests, yet survived the whole growing season with hardly any damage. The reason is that the plant on the left was given a gene taken from a common soil bacterium, which caused the plant to manufacture a simple protein that is harmless to humans and animals, and which has been approved by the EPA for use by farmers

for two decades, but has a deadly effect on these caterpillars. The protein, called B.t., or Bacillus thuringiensis, caused the hornworm, after a few bites of a tomato leaf, to stop feeding and eventually die. The plant survives.

That was test number one. There is the proof of it.

We tested two other types of tomatoes, and the results were just as dramatic. One type was made naturally resistant to the tobacco mosaic virus, which does very serious damage to tomatoes and other crops. Our transformed plants yielded 20 to 30 percent more than the control plants—that is by weight of product. The genetically altered plants thrived. Except for the addition of one gene, the tomato plants were in every respect the same as the unaltered control plants. The only difference that can be detected is that the protected plants yielded a significantly greater harvest.

The third type of plant was made resistant to Roundup®, what we believe is probably the most environmentally friendly herbicide anywhere. Roundup® is a nonselective herbicide, meaning it kills both weeds and desirable plants with equal effectiveness. By that, I mean when you put it on the ground it kills the weeds and it kills the plants. It takes everything out.

Roundup® does this by interfering with an enzyme that promotes growth in plants, and only in plants. We engineered the tomato plant to produce, if you will, an extra supply of its own enzyme, so that it would withstand the herbicide's activity. We sprayed the fields. The weeds died, and the tomatoes survived. To give you an example of the economic importance of Roundup® resistance, that experiment, the "Technology Review" magazine reported, not long ago, that California tomato farmers spend about $130 an acre controlling weeds. With Roundup®-resistant plants, their input costs would drop to—give and take—the $30 level an acre.

There is one other photograph I would like to show you. That is a petri dish with a human hand on the righthand side of it. That is what you are looking at.

[See page 77 for the photograph of the petri dish.]

Mr. HARBISON. The darker blue-green dots in the petri dish represent a uniquely significant advance in assuring that genetically engineered microorganisms can be released into the environment safely. As you know, bacteria can be precisely altered to possess characteristics of great benefit to crops and the farmers who grow them. They can protect against assault from diseases and insects.

But a valid question has been raised. Once released into the soil, can you monitor and track these bacteria? How long do they survive? How far can they migrate? The only way to answer those important questions was to develop a way to identify the altered organisms from the billions of bacteria that inhabit every gram of soil.

We have developed such a marker. Briefly, we have inserted marker genes into a common soil bacterium that causes the bacterium to turn bright blue under certain laboratory tests. That enables us to take soil samples, and detect one in a billion total organisms in a gram of soil.

We have received approval from the EPA to field test our marker gene system, and those tests began November 2 in collaboration with Clemson University. We have every reason to believe that these tests will be successful. CNN ran a minute, or so, story

on it yesterday morning, and "Time" magazine has come out with an article on it in its latest edition. "The Importance of Being Blue" is the headliner for it.

These are beneficial results and we are only beginning. But, the agricultural benefits of biotechnology will not be restricted to plants. We are going to improve animal husbandry as well.

Monsanto is but one of several companies—and we hope we are going to prove to be the best one—but nonetheless, others are hard at work at it, developing bovine somatotropin, or BST, as it is known in the industry, to increase the milk production efficiency of dairy cows. BST is a protein hormone produced naturally by cows.

It has been known since the 1920's that cows given additional amounts of BST become more efficient milk producers. But we had no practical way of obtaining sufficient quantities of BST until biotechnology taught us how to produce it with altered bacteria in fermentation tanks, as Dr. Thomas was addressing earlier. Now we can get pure and reliable supplies of BST.

This protein substance will not become a commercial reality until we have obviously completed the necessary safety and effectiveness tests required by the FDA. Already, FDA has authorized as safe for human consumption the milk and meat from BST-treated cows. Full regulatory approval awaits the completion of long-term cow health and efficiency studies, and those are now in progress.

We believe that BST should be a welcomed management tool for our dairy farmers. Because it causes cows to produce 10 to 25 percent more milk with a corresponding 5 to 15 percent improvement in feed efficiency, it will allow dairymen to lower their cost of production, and so raise their income. BST will favor the good dairy manager regardless of herd size. It is not a product devoted solely to the big farm. Unlike other dairy innovations of the past several decades such as milking machines or feed silos, BST will not be capital intensive.

As to its economic impact on dairying nationwide, a recent, and we believe comprehensive review by the USDA's Economic Research Service concluded that "since BST will be available to all operators and little additional capital or operational changes are required, BST should reinforce, but not fundamentally change, structural trends already underway" in the dairy industry."

BST should be good for consumers as well. BST is another technology in a long line of technologies in the dairy industry which has resulted in efficiency in production leading to a lower rate of price increase for milk as opposed to inflation. Over time, lower milk production costs ought to translate into milk and dairy products whose prices rise less rapidly than those of competing foods.

BST is going to be an option for dairymen worldwide. Our dairy farmers are going to need it in this country to remain competitive.

Another new product. Let me mention one more to you. The porcine analog of BST, called PST, or porcine somatotropin, I think also deserves your attention for just a moment. This product of biotechnology is like bovine somatotropin in its protein nature, its inherent human safety, and its method of manufacture. Hogs given supplemental PST channel more food energy into meat than they do into fat. That is what we are after, isn't it? Used in finishing

hogs, PST causes them to gain weight more rapidly, on less feed, and to produce a markedly leaner meat.

I have, Mr. Chairman, a few pictures of some porkchops, if you will——

Senator HARKIN. We are always interested in that out in Iowa.

Mr. HARBISON. As you can see in the picture, there is a marked increase in the loin of the pork with a corresponding decrease in the fat content. So, again, its beneficiaries will benefit both producers and consumers. PST is included on the list of Monsanto Company biotechnology research products.

[See page 78 for the photograph of the pork loin.]

Mr. HARBISON. The benefits of biotechnology to our health, to the environment, to our economy, become more clear with every new article published, every new field test begun, every new therapeutic tool submitted for approval.

It is not surprising, therefore, that governments such as the United Kingdom, Holland, and Japan—we could name a variety of others—have formally recognized biotechnology and genetic engineering as important to the economic futures of their nations.

They have targeted, if you will, the disciplines involved. They have organized for progress, and in some cases they have taken a major role in directing research, development, and commercialization.

In this country, by contrast, biotechnology is still perceived primarily as a regulatory and legal problem, not an economic opportunity. A regulatory structure has been fashioned that we believe is functioning quite well in assuring the public that the science of biotechnology is safe. Beyond the regulatory concerns, however, there is a political vacuum. Historically, I think it is fair to say that our country rarely, if ever, charts a long-term strategy for emerging technologies in order to assure they are properly recognized and supported, let alone to assure that they deliver the economic benefits they offer.

In other words, much effort is being expended to see that nothing goes wrong, but little effort is being expended to see that things go right.

What is the proper role of our Government in the development of this new industry? Well, that will get a lot of debate, I am sure, and should. But I believe that what we need is proactive leadership by the Government. Now you say, well, what does that mean? Let me give you a few examples, and they are by no means all-inclusive. We have a regulatory system that works. We need to allow that system to work and have the regulators continue to move, hopefully with alacrity, in their regulatory decisions based on science; we need a research budget for agriculture that will continue to support the development of our trained scientists and technicians. More emphasis on biotechnology. It receives a disproportionately low share of the total, in all likelihood.

We certainly need intellectual property protection. There is protection in the United States, but in our negotiations with other countries we need to ensure that intellectual property is protected in countries around the world.

Foreign based companies, such as the Japanese, for example, routinely visit small U.S! companies, and offer financial support for

the right to license the small companies' products in exchange for needed capital and manufacturing capability. You were addressing the subject earlier. We need to help small companies manufacture their products by providing trained personnel from our educational programs, and other incentives we can put there.

I have had personal conversations with the heads of some of these companies. Some of them have told me they literally get weekly visits from representatives of firms, in this case, Japan. They want to buy into those companies, 10, 15, 20 percent. Money is simply no object for that share of the company, and, in exchange, they want the technology of the company and the right to manufacture the products, not only for their home market but, indeed, for ours. It goes to the heart of the question you were asking earlier.

I do not have a range of simple answers to that. There are surely other needs we must address. I do not know them all. But we have a mix of large and small companies involved in this industry, and I think it would be most suitable to pull together a representational group of those companies, and sit down and discuss with them what are the needs, what are the problems they are facing, what issues do we have to address to keep competitive.

I do not believe we need new legislation. We do need good, sound, science based regulations, and I think we are well on the way to achieving that point. But I think over and above all, we need a commitment from policymakers to match the commitment that private industry is making to make this technology successful.

Good work is being done on issues that are important to us, such as patent law and intellectual property protection, at least in the United States—but there is something missing, and it is rather amorphous. It is hard to get your hands on. There is no atmosphere, no discernible official attitude toward this or any other emerging technology, for that matter, other than maybe the President's statement on superconductivity. The industry, and those who regulate it, are operating largely in a political vacuum. There is no clear signal from our political leaders, if you will, to "go for it." That is not what we put out. The consequences of such a signal are subtle, you will have a tough time writing them down, but they can be profound.

Let me offer an example, if I might. If a scientist in our company came to me and said, "I have this great idea to do further basic research in this field that could result in products of this nature."

And I said to him, "Well, that's very interesting. Let me tell you what I'm going to do for you. First, I'm going to put the tax people on you to see that you don't cheat. Secondly, I'm going to assign the lawyers to you to see that everything is done legally. Third, we'll have to watch the total regulation of it very carefully, and then I will put the controller on it as well and he'll watch over it."

My guess is I would never see him again. What I have to say to that man is: I think that is a great idea, I think you have something here. We are going to do this ethically, going to do it legally, going to do it intelligently. How can I help you? We never hear that. The first part we get. I think we have to change, and I think the change could be profound.

It is difficult for entrepreneurs, particularly the smaller ones, to operate in the vacuum we have created. They need to know—we all need to know—not just the entrepreneurs, but those of us in the bigger companies—that the rules of the game will not change, that we will not have to throw out our expensive test protocols, or endlessly rewrite the applications for product testing and approval for no good scientific reason. Entrepreneurs, large and small, need to know that their considerable financial risks are worth taking.

It is also difficult for the regulators who oversee the industry to operate in a vacuum. I think they do their scientific best, but it seems to me they need to know that Congress and the administration, cooperatively, will cope with valid issues like ethics, while at the same time supporting the process of the industry based solely on good science.

It is now time to recognize there are two sides to the risk-benefit equation. All of us, everyone in this room. Scientists, policymakers, environmentalists, naturalists, farmers, the sick, the chronically hungry. Every one is a stakeholder in biotechnology. It is going to impact us all as sure as we are alive. But too many of those who stand to benefit from this science simply do not realize it. They do not understand it. I like the idea of this country reaping the benefits from the technology it pioneered.

A few weeks ago, at the Industrial Biotechnology Association conference here in Washington, Bruce Merrifield, who is Assistant Secretary of Commerce for Productivity, Technology and Innovation, suggested that the Government should be the "proactive agent of change," and the catalyst for the development of this and other emerging technologies. Now a catalyst makes things happen without itself changing or consuming itself in the course of making things happen. I see the Government's role should not be that solely as a protector of the public health and welfare, but also as a supportive communicator and a participant in building public awareness and acceptance, and enthusiasm for the potential of this science.

It does not mean the Government ought to run the show, but it does mean good economic analyses, development of high-quality data bases, careful monitoring of other nations' competitive efforts. We have not done that now in almost 4 years. There has been no analysis of the biotechnology industry, that I know of, from Government since 1984. These are the first congressional hearings on the generic issue of biotechnology, that I am aware of, on this subject in this Congress. I salute you for that. I think you are right on the mark in doing it. Much can be done to help companies involved in this field understand their competitive situation, identify their market niches, steer their efforts in the right direction, and, above all, gain public understanding.

We have in our research facility in St. Louis some 123 chambers in which we can create literally any atmosphere we choose for our research and plant growth. We can provide any soil condition, temperature range, moisture and light level found anywhere on Earth. What I am suggesting today is for the Government in a way emulate that, to create an atmosphere of support and understanding for the biotechnology industry in this country.

This is one of, maybe the largest, in terms of economic impact, of the new technologies of the 1990's. The scientifically developed countries of the world are literally "pulling out all the stops" to develop the technology, and furthermore, to produce its products.

It is worth billions, countless billions, hundreds of billions in all likelihood. We had better take action to be sure we are in the front ranks. Thank you, Mr. Chairman.

[The prepared statement of Mr. Harbison, with attachments, follows:]

TESTIMONY OF

EARLE H. HARBISON, JR.
PRESIDENT AND CHIEF OPERATING OFFICER
MONSANTO COMPANY
ST. LOUIS, MISSOURI

NOVEMBER 4, 1987

Mr. Chairman, members of the Committee, thank you very much for inviting me to testify today. I am Earle H. Harbison, Jr., President and Chief Operating Officer of Monsanto Company. I am pleased to be here today, both as a representative of Monsanto, and as advocate for biotechnology.

Fifteen years ago, two American researchers were the first to splice a gene from one organism into the genetic material of another organism. Their efforts earned them the Nobel Prize in biology, and have brought us to what has been called "the brink of a new industrial revolution."

To the members of this Committee, I need not dwell on the basis for that remark. The contributions biotechnology can make to human health are by now obvious. For example, tissue plasminogen activator (tPA) in relieving heart attacks, human growth hormone, and human insulin. Many dozens of new diagnostic tools are on the market to aid in the early detection of disease. New therapies to treat disease, and new vaccines to prevent them, are also on the way, and offer hope of treating diseases

such as malaria and AIDS that cannot be reached with the traditional tools of medicine.

In agriculture, which is this Committee's jurisdiction and one of Monsanto's main areas of research, we believe that biotechnology offers the most exciting and dramatic prospect for improving the reliability and efficiency of farming since man first began tilling the soil.

The ability to provide the world's crops with added protection from insects, disease, and stresses is rapidly being demonstrated. Nature offers us a huge menu of beneficial traits developed through millions of years of evolution. We now know how to transfer some of those traits across species lines and will expand this knowledge in the future. We can do it rapidly, precisely, and with great predictability of results, as opposed to the random, time-consuming process of traditional plant breeding. The results will be an enormous increase in the efficiency and productivity of farming, and a substantial competitive edge for the country whose farmers are the first to receive these new products.

With your indulgence, I want to show you some examples of what I mean, drawn from our own work. It doesn't take a scientist to see the significance of what I would like to show you.

Last June, in a test field in southern Illinois, and after receiving approval from the Department of Agriculture, we planted three genetically altered types of tomato seedlings. The field was harvested in October, and the data are being compiled now, but this photo speaks for itself.

B

That tomato plant on the ~~left~~ right was stripped almost bare by caterpillars -- specifically, the tobacco hornworm, a large, homely, and ravenous caterpillar familiar to backyard gardeners. The plant on the ~~right~~ left was attacked by the same pests, yet survived the whole growing season with hardly any damage. The reason is that the plant on the ~~right~~ left was given a gene taken from a common soil bacterium, which caused the plant to manufacture a simple protein that is harmless to humans and animals, and which has been approved by the EPA for use by farmers for two decades, but has a deadly effect on these caterpillars. The protein, called B.t. (Bacillus thuringiensis), caused the hornworm, after a few bites of a tomato leaf, to stop feeding and eventually die. The plant survives.

We knew that this natural defense against pests worked in the laboratory. Now we know that it works in the field, and will work under real growing conditions for our farmers.

We tested two other types of tomatoes, and the results were just as dramatic. One type was made naturally resistant to the tobacco mosaic virus, which does serious damage to tomatoes and other crops. Our transformed plants yielded 20% to 30% more than the control plants. The genetically altered plants thrived. Except for the addition of one gene, the tomato plants were in every respect the same as the unaltered control plants. The only difference that can be detected is that the protected plants yielded a significantly greater harvest.

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The third type of plant was made resistant to Roundup®, probably the most environmentally friendly herbicide. Roundup® is non-selective, meaning it kills both weeds and desirable plants with equal effectiveness.

Roundup® does this by interfering with an enzyme that promotes growth in plants -- and only in plants. We engineered the tomato plant to produce an extra supply of its own enzyme, so that it would withstand the herbicide's activity. We spraved the fields. The weeds died, and the tomatoes survived. To give vou an example of the economic importance of Roundup® resistance, *Technology Review* magazine reports that California tomato farmers spent $130 an acre controlling weeds. With Roundup®-resistant plants, their input costs would drop to just $30 an acre.

There is one other photograph I would like to show you. Monsanto has been able to develop a marker system to track genetically engineered bacteria in soil. The blue-green dots in the petri dish represent a uniquely significant advance in assuring that genetically engineered microorganisms can be released into the environment safely. As you know, bacteria can be precisely altered to possess characteristics of great benefit to crops and the farmers who grow them. They can protect against assault from insects and diseases.

But a valid question has been raised. Once released into the soil, can these be monitored and tracked? How long do they survive? How far can they migrate? The only way to answer those important questions was

to develop a way to identify the altered organisms from the billions of bacteria that inhabit every gram of soil.

We have developed such a marker. Briefly, we have inserted marker genes into a common soil bacterium that causes the bacterium to turn bright blue under certain laboratory tests. That enables us to take soil samples, and detect one in a billion total organisms in a gram of soil.

We have received approval from the EPA to field-test our marker gene system, and those tests began November 2 in collaboration with Clemson University. We have every reason to believe that these tests will prove successful.

These are beneficial results and we are only beginning. But, the agricultural benefits of biotechnology won't be restricted to plants. Animal husbandry will be improved as well.

Monsanto is one of several companies -- we hope we'll prove the best company -- developing bovine somatotropin or BST to increase the milk production efficiency of dairy cows. BST is a protein hormone produced naturally by cows.

It's been known since the 1920's that cows given additional amounts of BST become more efficient milk producers. But we had no practical way of obtaining sufficient quantities of BST until biotechnology taught us how to produce it with altered bacteria in fermentation tanks. Now pure and reliable supplies of BST are possible.

This protein substance won't become a commercial reality until we've completed the necessary safety and effectiveness tests required by the FDA. Already, FDA has authorized as safe for human consumption the milk and meat from BST-treated cows. Full regulatory approval awaits the completion of long-term cow health and efficiency studies now in progress.

BST should be a welcomed management tool for our dairy farmers. Because it causes cows to produce 10% to 25% more milk with a corresponding 5% to 15% improvement in feed efficiency, it will allow dairymen to lower their cost of production, and so raise their income. BST will favor the good dairy manager regardless of herd size. Unlike other dairy innovations of the past several decades, such as milking machines or feed silos, BST will not be capital intensive.

As to its economic impact on dairying nationwide, a recent, comprehensive review by USDA's Economic Research Service concluded that "since BST will be available to all operators and little additional capital or operational changes are required, BST should reinforce, but not fundamentally change, structural trends already underway" in the dairy industry.

BST should be good for consumers as well. BST is another technology in a long line of technologies in the dairy industry which has resulted in efficiency in production leading to a lower rate of price increase for milk to the consumer than inflation. Over time, lower milk production

costs ought to translate into milk and dairy products whose prices rise less rapidly than those of competing foods.

BST will be an option for dairymen worldwide. Our dairy farmers will need it to remain competitive.

The porcine analog of BST, called PST or porcine somatotropin, also deserves a mention. This product of biotechnology is like bovine somatotropin in its protein nature, its inherent human safety and its method of manufacture. Hogs given supplemental PST channel more food energy into meat than fat. Used in finishing hogs, PST causes them to gain weight more rapidly on less feed and to produce a markedly leaner meat. As seen in this picture, there is a marked increase in the loin of the pork with a corresponding decrease in the fat content. So, again, its beneficiaries will benefit both producers and consumers. PST is included on the list of Monsanto Company biotechnology research products.

I hope that this brief demonstration shows why we find the promise of biotechnology in agriculture so exciting. The effect on the economics of farming ultimately will be substantial. The first practical application of the research will be to reduce the costs of production. This increased efficiency a farmer enjoys will not be a function of farm size, but of farm management. Thus both small and large farmers who are good managers will benefit. Biotechnology will benefit the better managers most.

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With our nation and others already awash in agricultural surpluses, the question has been raised whether biotechnology will only make matters worse. My first answer to that is that production is a function of policy, not technology. It may be difficult to change policies, but it is impossible to stop progress on a global scale. These new products will be developed by someone, somewhere, and the world's farmers will decide whether to use them on the basis of their own economic considerations. Farmers of tomorrow will either use the products of biotechnology, or compete with those who do.

Incidentally, there has always been a concern about the effect of technology on farmers. Concern was raised about the effect of tractors versus animals to pull plows, about milking machines versus hand milking.

My second answer to that is that the road to future competitiveness and success in agriculture, both on the individual and on the national level, will be based on improvements in the cost of production. The individual farmer will use these advances to make their agricultural products cheaper to produce and therefore to buy.

Additionally, the science has the capability to make agricultural products more nutritious, better in quality. The global marketplace does not bother to ask a grain salesman how much he has. The questions are: How good is it, and how much is it?

A British dairy farmer, for example, operates under a quota system. He can sell only so much milk. He will use BST not to increase his

production, but to fine-tune his operations, making sure he produces right up to his quota, and cutting his feed-to-milk ratio so that he can pocket more profits.

In the United States, there are 50 percent fewer cows and 95 percent fewer dairy farmers than there were in 1955 and they produce more milk than we need. No new technology can make much of a change in that picture. How many dairymen will be milking in the future depends upon Government policy. How many will remain in business will depend upon their management skills, the availability of technology and Government policy. So, technology must be viewed as positive. I am not here today to talk about agricultural policy nationally and globally, but I want you to know that we feel these issues must be addressed, and that our company will cooperate with you in any way we can.

The benefits of biotechnology to our health, to our environment, and to our economy become more clear with every new research article published, every new field test begun, every new therapeutic tool submitted for approval. All of industry will feel the effects of the biology. From the leaching of minerals out of ores to the removal of toxic wastes from water, all the way to the manufacture of biodegradable plastics from corn stalks, the possibilities seem endless.

It is not surprising, therefore, that governments such as the United Kingdom, Holland and Japan have formally recognized biotechnology and genetic engineering as important to the economic futures of their nations. They have targeted the disciplines involved, organized for

progress, and in some cases taken a major role in directing research, development and commercialization.

In this country, by contrast, biotechnology is still perceived primarily as a regulatory and legal problem, not an economic opportunity. A regulatory structure has been fashioned that is functioning quite well in assuring the public that the science of biotechnology is safe. Beyond the regulatory concerns, however, there is a political vacuum. Historically, I think it is fair to say that our country rarely charts a long-term strategy for emerging technologies in order to assure they are properly recogized and supported, let alone to assure that they deliver the economic benefits they offer.

In other words, much effort is being expended to see that nothing goes wrong, but little effort is being expended to see that things go right. To put it still another way, most of the Nobel Prizes in genetic engineering are here, but not enough is being done to assure that the industry they create will be found here, too.

This year's winner of the Nobel Prize in economics, MIT's Robert Solow, was honored for his work in demonstrating the importance of technology to economic growth. In the 30 years since he did his pioneering research, we have seen the key ingredient in manufacturing shift rapidly from labor and materials to knowledge. According to Peter Drucker, writing in *Foreign Affairs* last year, 70 percent of the manufacturing cost of a semiconductor microchip is knowledge -- the research, development and testing that went into it. Materials account

for only three percent of the cost. Fifty percent of the cost of a prescription drug is knowledge. "In all developed countries," Drucker wrote, "knowledge workers have already become the center of gravity of the labor force."

The emerging industries of today are knowledge-based, replacing the materials-based industries that drove our economy for the first three-quarters of this century. In a recent report entitled "The Status of Emerging Technologies: An Economic/Technological Assessment to the Year 2000," the Department of Commerce found the most promising technologies in terms of their economic impact to be advanced materials, biotechnology, electronics, computing and automation. It is in those areas where we will find our future economic growth and our future competitiveness. Unlike materials-based industries such as steel or autos, these emerging industries produce not only products for export, but knowledge for export, in the form of licenses, royalty fees and services. "Exporting knowledge," Drucker wrote, "may actually create substantially more jobs than exporting goods."

Those are among the reasons why my company has invested about a billion dollars in bricks and mortar, equipment and, most important, the people in order to build a solid capability in biotechnology.

And that is why hundreds of small to medium sized companies have sprung up in the United States in recent years to pursue this technology. One does not have to be a Monsanto to pursue a good idea in this sort of industry. Those who have toured our Life Sciences Research Center near

St. Louis, as some of you have, see no giant machines or huge manufacturing facilities. The secret ingredients are people and capital. Protein sequencers cost a lost, but it is the scientists and the technicians who run them who count. No country can generate the basic knowledge and the capital needed to create a new industry the way the United States can. In biotechnology, as in most other knowledge-based enterprises, the translation of an idea to an economic reality can be done anywhere, on any scale.

There is, therefore, no reason why the United States should not continue to be a world leader in biotechnology and genetic engineering. The Government's huge investment in basic research is basic to America's economic future.

But good science is not enough. It is a long road from the lab bench to the marketplace. New technologies can be replicated rapidly these days. The key to Japan's success has been its ability to buy into our knowledge, then out-run us to the market. It happened in electronics, and Japan is hoping to make it happen again in biotechnology.

In England the newly formed Advisory Committee on Science and Technology reports to the Prime Minister.

All across Europe, active programs in biotechnology are developing, with the enthusiastic support of government.

In emerging countries such as Brazil, technology is being looked to as a means for them to enlarge their niche in the global agricultural market.

What is the proper role of our Government in the development of this new industry? What we need is proactive leadership by the Government. Let me give you just a few examples. We have a regulatory system that works. We need to allow that system to work and to have the regulators continue to move with alacrity in their regulatory decisions based on science; we need a research budget for agriculture that will continue to support the development of our trained scientists and technicians; we need intellectual property protection. There is protection in the U.S. but in our negotiations with other countries we need to ensure that intellectual property is protected in countries around the world.

Foreign based companies such as the Japanese companies are routinely visiting small U.S. companies and offering financial support for the right to license the small companies' products in exchange for needed capital and manufacturing capability. We need to help small companies manufacture their products by providing trained personnel from our educational programs. I was told by the CEO of a small company that he is visited almost weekly by representatives of Japanese firms offering money in return for that company's ideas and inventions. No questions asked. In return, the Japanese companies will manufacture and distribute the products.

Let me suggest that you pull together a panel of large and small company executives who can help you find out what is needed.

We do not need new legislation. We do need good, sound, science-based regulations, and I think we are well on the way to reaching that point. But mostly, we need commitment from policymakers to match the commitment private industry is making.

Good work is being done on issues important to us, such as patent law and intellectual property protection. But there is something missing. There is no atmosphere, no discernable official attitude toward this or other emerging technologies. The industry, and those who regulate it, are operating largely in a political vacuum. There is no clear signal from our political leaders to "go for it." The consequences of such a signal are subtle, but can be profound.

It is difficult for entrepreneurs, particularly the smaller ones, to operate in a vacuum. They need to be sure that the rules of the game will not change, that they won't have to throw out their expensive test protocols, or endlessly rewrite their applications for product testing and approval for no good scientific reason. Entrepreneurs large and small need to know that their considerable financial risks are worth taking.

It is also difficult for the regulators to operate in a vacuum. As they do their scientific best, they need to know that Congress and the

Administration cooperatively will cope with valid issues like ethics, while at the same time supporting the progress of the industry.

By now, all the doomsday scenarios imaginable have been thrown at the new biology, and are being answered by a solid track record of safety -- based on science -- built up over the last fifteen years.

We all agree that the public must be protected, and we all agree that the public must perceive that it is being protected. It is now time to recognize that there are two sides to the risk-benefit equation. All of us -- scientists, policymakers, environmentalists, naturalists, farmers, the sick and the chronically hungry -- are stakeholders in biotechnology. But too many of those who stand to benefit from this new science do not realize it.

If I can offer one concrete example, a cotton farmer has to spray his crop at least a half-dozen times a season to protect it from pests. What would be the effect on his input costs, and therefore his profitability, if he were provided with a strain of cotton naturally resistant to the major insect pests? What would be the effect on his competitiveness in the marketplace if he could cut his costs of production? And what would be the effects on the environment?

The benefits of biotechnology cascade through the economic system. There is no doubt that someone will provide American farmers with the technology to increase his efficiency, improve his profitability, and protect his and our environment. I would like for that someone to be an

American company, and because I like the idea of this country reaping the benefits from the technology it pioneered.

A few weeks ago, at an Industrial Biotechnology Association conference here in Washington, Bruce Merrifield, who is Assistant Secretary of Commerce for Productivity, Technology and Innovation, suggested that the Government should be the "pro-active agent of change," and the catalyst for the development of this and other emerging technologies. I fully support this position. A catalyst, if I remember my high school science, makes things happen, without itself changing or being consumed in the course of things. I see Government's role not solely as a protector of the public health and welfare, but also as a supportive communicator and a participant in building public acceptance and enthusiasm for achieving the potential of biotechnology.

That does not mean running the show. It does mean good economic analyses, high-quality data bases, careful monitoring of other nations' competitive efforts. There has been no analysis of the biotechnology industry from Government since 1984. These are the first Congressional hearings on the generic issue of biotechnology in this Congress. Much can be done to help the companies involved in this field understand their competitive situation, identify their market niches, steer their efforts in the right direction, gain public understanding. And I am convinced that the U.S. industry will move forward benefitting mankind and the economy if it knows that the Government wants this and other emerging technologies to succeed and reach the global marketplace as rapidly as good science and sound regulation permit.

At our research facility in St. Louis, there are 123 chambers that can create any atmosphere we choose for our research in plant growth. We can provide any soil condition, temperature range, moisture and light level found anywhere on earth. What I am suggesting today is for the Government to do the same -- create an atmosphere of support and understanding for the biotechnology industry in the United States.

PATRICK J. LEAHY, VERMONT, CHAIRMAN
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DAVID K. KARNES, NEBRASKA

United States Senate
COMMITTEE ON
AGRICULTURE, NUTRITION, AND FORESTRY
WASHINGTON, DC 20510-6000

November 23, 1987

Earle Harbison, Jr.
President and Chief Operating Officer
Monsanto Company
800 North Lindbergh Blvd.
St. Louis, Missouri 63167

Dear Mr. Harbison,

Thank you for participating in the joint hearing on biotechnology held by the Agriculture Committee and the Judiciary Subcommittee on Technology and the Law.

Enclosed are written questions to which members of the Committees would like you to respond. As I mentioned at the conclusion of the hearing, the questions and answers will be included as part of the permanent hearing record.

Please respond to these questions by December 14, 1987. If you have any questions, please contact Kathleen Merrigan, Senate Agriculture Committee Staff at (202)224-5207 or Marc Rotenberg, Counsel to the Subcommittee at (202)224-3406.

I appreciate your assistance in compiling a complete record on the issues before the Committees.

Sincerely,

Patrick J. Leahy

PATRICK J. LEAHY
Chairman

CC: Chester Dickerson, Jr.

QUESTIONS FROM COMMITTEE MEMBERS
FOR MR. EARLE HARBISON

NOVEMBER 4, 1987 HEARING ON BIOTECHNOLOGY

Questions from Senator Leahy

1. We have the world's premier biomedical research system, anchored by the National Institutes of Health. Should we have a similar national institute dedicated to agricultural research or biotechnology in general?

2. How can we ensure that we have adequate human resources to transform the promise of new biotechnologies into economic growth?

   a. What steps need to be taken to provide the necessary training and retraining of employees in biotech industries?

   b. Should we do more to encourage engineers in manufacturing and product delivery, as opposed to basic research?

   c. Should we encourage the training of American students abroad in countries such as Japan?

3. What do we have to fear from the release of biotech products into our environment? How serious is the threat? What measures should we take to protect our environment?

4. Are there areas of biotechnology that we should decide right now not to pursue? What are the dangers if we do pursue developments in these areas?

5. What role do small firms play in biotechnology innovation? How do we ensure their survival in the biotech craze? Are people right to worry that in 10 years there will be only 4 or 5 giant firms controlling biotechnology in this country?

6. How do we involve the general public in the biotechnology decision-making process in a meaningful way?

7. Do you agree with the National Academy of Sciences finding that we need to infuse our basic research with $500 million annually? If this figure is unrealistic, what figure would you suggest and where should we direct our support?

8. The Europeans and Japanese have undertaken many cooperative efforts and joint research programs such as EMBO,

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EUREKA, and BRAIN. What comparable programs can or should be developed in the United States?

9. Will biotechnology promote the loss of biodiversity, as we develop highly specialized crops and animals? What can we do to lesson the risks?

10. Do you think it is possible to reach an international agreement on research safety guidelines for biotechnology? Would such an agreement be enforceable? How should we begin the process?

Questions from Senator Conrad

1. What are the key reasons that new research ideas are not developed into marketable products? In your response, please include your thoughts on whether it is difficult to find investors and members of the financial sector willing to finance this development, and whether companies are hesitant to invest long-term capital and resources into the development and refinement of new research products? What kind of governmental financial assistance would be helpful to companies and individuals trying to commercialize new biotechnological products?

2. In the 1970s, the U.S. was the leader in basic research on semiconductors. Today, we are struggling to keep up with the semiconductor manufacturing capabilities of Japan. How can we prevent a similar decline in our current lead in the biotechnology field?

3. Would it be useful to set up a council which would act as a liaison between private and public researchers, and the academic, industrial, the financial sector, and marketing sector? Such a council would help these sectors explore and develop the potential for producing new products.

4. If the federal government should take a role in helping compainies through the developmental stage of product commercialization companies and projects and assure that any available federal funds are directed at the most promising areas of agricultural biotechnology?

5. Monsanto produces BST in Australia. Do our regulations make it disadvantagous for your company to produce the hormone in the United States?

Questions from Senator Karnes

1. Do you feel that the United States is on the leading edge of this technology?

2. What do you consider to be the most productive area of biotechnology up to this point?

3. Where do you see biotechnology taking us in the next ten years in terms of tangible benefits?

4. How has the government helped or hindered Monsanto's research efforts?

5. What do you feel we can learn from other high technology areas which are undergoing rapid development?

Questions from Senator Harkin

1. What types of support do other countries provide to their business concerns in support of bringing new research based products on line? What are other countries doing that you believe the U.S. should adopt to better provide financial resources for their research companies in the area of biotechnology?

2. We cannot reasonably expect any profit making company to take basic research results and try to make use of it in a direction that is highly risky and where the results will not be known for 10 or 15 years. Given that reality, where should the government's role stop and the private company's role begin?

3. What are the barriers to university-company cooperation in biotechnology research that you believe should be modified?

4. If you were the sole decider of what should be done in the area of patents, how would you change the present system as it applies to biotechnological products so as to fairly reward creativity?

5. How would you modify our regulatory framework that would provide protection for our environment and improve the ability to efficiently conduct biotechnology research.

6. Do you perceive that there is sufficient federal funding directed towards the goal of diversifying our nation's agriculture towards non-food products?

Questions from Senator Boschwitz

1. How important is the private sector for biotechnology research and development?

2. How important is small business for biotechnology research and development?

3. To what extent does present and proposed FIFRA legislation affect biotechnology research and development?

4. Would Federal, State and local regulations that increase the risks and costs of biotechnology research and development have an impact on the competitiveness of U.S. business?

5. Please itemize current and proposed legislation that would hamper or reduce the participation of small business in biotechnology research and development with particular emphasis on current and proposed FIFRA legislation. Please include comments or analysis on how agrochemical companies may or may not reduce biotechnology efforts should their present chemical based products be made less profitable or should strict and expensive regulation inhibit the development, manufacture and marketing of chemical agricultural products.

Monsanto

EARLE H. HARBISON, JR.
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Phone (314) 694-3008

December 18, 1987

The Honorable Patrick J. Leahy
United States Senate
433 Senate Russell Office Building
Washington, D. C. 20510-4501

Dear Pat:

Enclosed are our answers to the questions you and your committee submitted to us. I hope you find them responsive and, more than that, helpful.

My colleagues and I are certainly prepared to help your committee in any way we can to further your deliberations on the important issue of the economic potential of biotechnology. I sense from our discussions that we share a common goal, namely, to bring the realization of the benefits of that technology to our people as fast as good science and sound regulation permit.

As I said in my testimony, the creation of a panel of executives from large and small companies could be of benefit in helping you find out what is needed to reach our goal of having the U.S. be competitive internationally. Our own soundings within industry indicate strong support for this concept. The task before us requires teamwork if the United States is to maintain its advantage in this rapidly developing global industry.

I look forward to the prospect of pursuing this concept further with you. If you believe such a panel would be helpful, please let me know and I will be glad to work with your staff. And allow me to extend again an invitation to you, your colleagues and your staff to visit our research facilities.

Sincerely,

Best wishes for a happy holiday season!

EHO

Enclosure

EARLE H. HARBISON JR.

SENATE COMMITTEE QUESTIONS

QUESTIONS FROM SENATOR LEAHY

1. We have the world's premier biomedical research system, anchored by the National Institutes of Health. Should we have a similar national institute dedicated to agricultural research or biotechnology in general?

   A Agricultural research needs improvement but I am not certain that a National Institute of Agriculture is needed. The USDA should develop a much more powerful peer reviewed extramural program so that the best research scientists in land-grant colleges and elsewhere could compete for research funds to answer important questions. A national institute for biotechnology is definitely not needed.

2. How can we ensure that we have adequate human resources to transform the promise of new biotechnologies into economic growth?

   a. What steps need to be taken to provide the necessary training and retraining of employees in biotech industries?

   b. Should we do more to encourage engineers in manufacturing and product delivery, as opposed to basic research?

   c. Should we encourage the training of American students abroad in countries such as Japan?

   A Funding for graduate fellowships and post-doctoral fellowships by the National Science Foundation, NIH, and the USDA would be enormously valuable. Training funds are in short supply. High school curricula include very little material on the new biology. The whole infrastructure of education has to be assessed to make it more capable of producing the qualified people to make the knowledge-based industries that will be the strength of our future economy.

   In addition to our strength in basic research, the United States needs to develop enhanced capabilities in the area of process technologies. Nations such as Japan are often more capable of taking our ideas and inventions and developing them than we are. We need engineers, particularly with advanced degrees in biological sciences combined with engineering skills.

   There needs to be continued emphasis in the basic education and training of our students to satisfy the rapidly increasing need for talent in knowledge industries such as biotechnology. In some areas of research and engineering, the number of foreign citizens in U.S. postdoctoral programs approaches 50 percent. The number of Americans doing advanced studies in other

countries is very low. Intellectual exchange should be a two-way street. We have much to learn from other nations. Greater emphasis in language skills to permit our students to have an equal footing in foreign countries should be a priority.

3. What do we have to fear from the release of biotech products into our environment? How serious is the threat? What measures should we take to protect our environment?

A The National Academy of Sciences' recent report answers this question decisively. Society has no need to fear the release of biotechnology products in the environment. Society does have reason to be concerned about the importation of exotic plants and animals which might compete with local plants and animals. Quarantine regulations handle this today and are adequate.

Also, fifteen years of research in genetic engineering without incident support the National Academy of Sciences' conclusion that no unique hazard is presented by this technology. Nevertheless, any new industry should have the proper procedures and scientifically based regulations in place to ensure protection of the environment and human health. I believe the Coordinated Framework for the Regulation of Biotechnology provides the road map to regulation of biotechnology. The level of caution in biotechnology, established before the fact, is unique in the history of technology.

4. Are there areas of biotechnology that we should decide right now not to pursue? What are the dangers if we do pursue developments in these areas?

A At this time, the only area of biotechnology that should not be pursued is the application of biotechnology to human germ cells -- eggs and sperm -- to alter the heredity of future generations. No one has proposed this at present, but it is an issue about which the public at large is concerned.

5. What role do small firms play in biotechnology innovation? How do we ensure their survival in the biotech craze? Are people right to worry that in 10 years there will be only 4 or 5 giant firms controlling biotechnology in this country?

A The role of small firms in biotechnology is critical to the eventual maturing and economic success of the industry. Right now, there are more worthwhile ideas to be pursued than there are companies and people to pursue them. Even large companies such as Monsanto cannot develop all the ideas they come up with. This is an industry particularly suited to entrepreneurism, where one individual with a good idea can develop it with modest capital expenses.

Ten years from now there still will be hundreds of U.S. companies engaged in biotechnology. These small companies play a crucial role in innovation, and they seem to be surviving very well. It is our perception that there is enough venture capital. But Monsanto is a large company. I think that a panel of large and small companies ought to be convened so that the committee can hear from them, large and small.

One thing that could be done to help ensure the survival of small and large companies is to make certain that regulatory procedures are based on scientific prudence and not change for change sake because change is expensive and creates uncertainty, causes delays and escalating of costs using up the limited resources of companies.

6. How do we involve the general public in the biotechnology decision-making process in a meaningful way?

A In a sentence -- increased public awareness and education. The general public will make the ultimate decision about the success of biotechnology, by its acceptance of its products. That climate of acceptance will not develop without a systematic program of information transfer. Industry, academia, the government and the stakeholders in biotechnology must do a better job of communicating the safety, the benefits and the economic importance of biotechnology. The public will make the right decisions, but only if it is fully informed.

7. Do you agree with the National Academy of Sciences' finding that we need to infuse our basic research with $500 million annually? If this figure is unrealistic, what figure would you suggest and where should we direct our support?

A Yes, $500,000,000/year is a minimal figure if this nation is to compete with Japan and Europe in an economy which is increasingly becoming knowledge intensive rather than natural resource intensive. Equipping the scientific laboratories in universities and enhancing opportunities for graduate training are key areas.

8. The Europeans and Japanese have undertaken many cooperative efforts and joint research programs such as EMBO, EUREKA, and BRAIN. What comparable programs can or should be developed in the United States?

A The National Science Foundation has a range of programs that are already being developed. Examples are the Engineering Research centers and the Science and Technology Centers located at universities. The MIT bioprocessing center is an example of the latter program. Also, there are centers which bring together consortia of universities, national laboratories and the private sector.

9. Will biotechnology promote the loss of biodiversity, as we develop highly specialized crops and animals? What can we do to lesson the risks?

A Biotechnology will increase biodiversity and not decrease it. It provides the opportunity to create new germ plasm and new varieties of plants. Unlike conventional plant breeding which narrows the germ plasm base and diversity, biotechnology enables genes to be moved from diverse organisms into crops, for example, and thus enlarges the germ plasm base. Biotechnology will enable us to design crops easily to meet particular climate and soil conditions and lead to crops that are well tailored to particular geographic areas and agricultural practices. I anticipate an increase in crop diversity, not a decrease.

10. Do you think it is possible to reach an international agreement on research safety guidelines for biotechnology? Would such an agreement be enforceable? How should we begin the process?

A The NIH RAC guidelines are almost universally used as safety guidelines for recombinant DNA experiments. Also, the U.S. Coordinated Framework for the Regulation of Biotechnology references the OECD guidelines on biotechnology testing. The international regulation of biotechnology is still being discussed by the OECD and SEC and U.S. regulators. There is a great deal of work underway to ensure compatible international regulation.

QUESTIONS FROM SENATOR CONRAD

1. What are the key reasons that new research ideas are not developed into marketable products? In your response, please include your thoughts on whether it is difficult to find investors and members of the financial sector willing to finance this development, and whether companies are hesitant to invest long-term capital and resources into the development and refinement of new research products? What kind of governmental financial assistance would be helpful to companies and individuals trying to commercialize new biotechnological products?

A It is our understanding that there is sufficient venture capital and that government financial assistance is not needed.

I suggest that a panel of large and small company executives could help provide insight to the needs of companies in a range of sizes. What is needed is advocacy by public officials. The American public should be made aware that its leading senators and congressmen see biotechnology as a valuable technology important for America's economy and the health of her citizens.

A reason why new research ideas sometimes do not reach the marketplace is an uncertain regulatory environment resulting in

the loss of the competitive edge. Twists and turns in the regulatory atmosphere by changing or repeatedly adding to regulations at the Federal level can seriously slow progress to the point where the research is abandoned or is completed by someone operating in a more stable regulatory atmosphere. This causes a loss of the competitive edge in a global research effort. The United States suffers no lack of venture capital.

2. In the 1970's, the U.S. was the leader in basic research on semiconductors. Today, we are struggling to keep up with the semiconductor manufacturing capabilities of Japan. How can we prevent a similar decline in our current lead in the biotechnology field?

A Continue adequate support of NIH and NSF so that university research in biotechnology can continue. Also, ensure that there are no unreasonable regulatory obstacles in the way of commercializing the products of biotechnology. Great credit must be given to the Japanese for the willingness to buy into new technologies, and their skill at developing them. They simply beat us to the marketplace in electronics. The same could happen in biotechnology because of their skills at scale-up, and -- more important -- because of their determination to do so. The concept of determination to win is decisive. That commitment requires the participation of policymakers. But specifically, there must be protection of intellectual property globally.

3. Would it be useful to set up a council which would act as a liaison between private and public researchers, and the academic, industrial, the financial sector, and marketing sector? Such a council would help these sectors explore and develop the potential for producing new products.

A No. There are already many, many organizations at regional, state and individual university and company levels that address those issues.

4. If the federal government should take a role in helping companies through the developmental stage of product commercialization companies and projects and assure that any available federal funds are directed at the most promising areas of agricultural biotechnology?

A I don't believe the Federal Government should be involved in helping companies through the developmental stage of product commercialization, but I represent a large corporation. It would be useful for you to speak to heads of smaller, embryonic companies and see what their view is and what help they might believe the Government could give them. Certainly, our outstanding science-based institutions such as the National Science Foundation, National Academy of Science and National Institute of Health do not address the large and complex technical-commercial-regulatory issues involved in taking an idea from the laboratory to the marketplace or to the farmer. This process can take between four to twelve years.

With regard to directing Federal funds at the most promising areas of agricultural biotechnology, I believe the Department of Agriculture should shift some of its current funding from more traditional programs to biotechnology. I don't know whether we are suffering so much from a shortage of funds as an unenlightened allocation of them.

5. Monsanto produces BST in Australia [sic]. Do our regulations make it disadvantageous for your company to produce the hormone in the United States?

A Monsanto produces BST in Austria because it was not possible, under previous legislation, which was changed in the 99th Congress, to produce the product in the United States and sell it in Europe before it was cleared in the United States. The clearance for pharmaceutical products and products like BST for animals is much more rapid in Europe than in the United States. This country's competitiveness in biotechnology would be enormously enhanced if the regulatory agencies -- FDA, EPA, USDA -- had resources and an incentive to move products forward more rapidly.

QUESTIONS FROM SENATOR KARNES

1. Do you feel that the United States is on the leading ledge of this technology?

A The United States is far and away the world leader in this technology, but other countries are rushing to catch up, especially Japan and in Europe, England, France and Germany to name a few. We can maintain our lead if we do everything we can to let this technology develop as rapidly as good science and sound regulations permit.

2. What do you consider to be the most productive area of biotechnology up to this point?

A Applications of biotechnology to curing human diseases have been the most important results of biotechnology thus far. During the next five years, human health will be vastly improved by new drugs such as TPA for heart attacks, erythropoetin for anemia, human growth hormone for dwarfism, vaccines for hepatitis and malaria and ultimately vaccines for AIDS. But I believe that before this century is over, agricultural biotechnology, particularly crop genetics crop-enhancing microorganisms, will be tremendous and there are an array of products already in the pipeline.

3. Where do you see biotechnology taking us in the next ten years in terms of tangible benefits?

A During the next ten years we will see many more diseases cured and enormous benefits to agriculture. The tangible benefits from biotechnology will, of course, be concentrated on new methods for the treatment and prevention of disease, including AIDS, and the greatly increased reliability of the global harvest. In the United States, I foresee a greatly improved competitive position for our farmers -- both in their ability to sell their products overseas and to compete with food imports. For the nation's economy as a whole, a tangible benefit will be the development of a new growth industry which can rival computers, electronics and the steel industry in its heyday -- if we maintain our competitive edge.

4. How has the government helped or hindered Monsanto's research efforts?

A Public support of academic research and the ability of our researchers in this country to pursue their intellectual interests has benefited all sectors of American industry. Thus, Monsanto has shared in this benefit. But, what should be appreciated is the fact that from the time a basic discovery is made until it reaches the marketplace involves from four to twelve years, much technical development, and significant resources.

5. What do you feel we can learn from other high technology areas which are undergoing rapid development?

A I think the most important lesson we can learn from other rapidly developing areas of high technology is that the United States no longer has a corner on new technologies. The U.S. spends ten times more on basic research than any other country, but new technologies can be rapidly replicated now. It is not only the fully industrialized countries, but developing nations which are demonstrating the ability to adopt technology developed here and push it rapidly to commercial success. The velocity with which technology transfers globally cannot be slowed, nor should it be. But the velocity with which we develop our own technologies must be increased. Basic research is a matter of national policy. The development of promising new industries is not. Our national commitment would be invaluable. It's as simple as that.

QUESTIONS FROM SENATOR HARKIN

1. What types of support do other countries provide to their business concerns in support of bringing new research based products on line? What are other countries doing that you believe the U.S. should adopt to better provide financial resources for their research companies in the area of biotechnology?

A According to a recent Department of Commerce report on "Biotechnology in Western Europe," all European countries

provide basic research support, and most provide applied research funding to both universities and industry. In addition, Sweden, the Netherlands, the U.K. and Germany provide risk capital, and all those plus France offer loans and grants. The approach adopted by other nations is not necessarily relevant to the U.S.

In Europe and Japan, the industrial base is small, concentrated in a few major firms, which places a heavier burden on the national government to see that promising areas of research and development are pursued. The important point is that seven European countries and Japan have or are considering establishing national programs in biotechnology.

As the report states: " In addition to increases in funding support and changes in the structure of the research establishment, national programs also serve an important function in establishing political consensus in support of biotechnology... The pace of industrial development in biotechnology is set by government policy."

Certainly R&D tax credits are vital to start-up firms in this industry. We also feel very strongly that universities need much more help if they are to turn out both the research and the talent needed to develop emerging technologies. Beyond that, we feel that it is more important for the government to create a climate that will encourage new ventures and the risk capital to fund them than to provide the money itself from tax revenues.

2. We cannot reasonably expect any profit making company to take basic research results and try to make use of it in a direction that is highly risky and where the results will not be known for 10 or 15 years. Given that reality, where should the government's role stop and the private company's role begin?

   A First, Monsanto does take a 10- to 15-year look at our research investments. We began our investment in biotechnology research over 15 years ago and hope to have our products in the marketplace next year. The government should continue to fund research in America's great research universities so that basic research is done effectively. Reliable support for NIH and NSF is crucial. Companies will take 10- and 15-year risks if intellectual property will be protected. Long-term protection for intellectual property is crucial.

3. What are the barriers to university-company cooperation in biotechnology research that you believe should be modified?

   A I see no real barriers to university-company cooperation in biotechnology research. Monsanto has research agreements with many universities such as Washington University in St. Louis, Clemson University in South Carolina and other great institutions.

Both the universities and Monsanto have profited with these research agreements.

4. If you were the sole decider of what should be done in the area of patents, how would you change the present system as it applies to biotechnological products so as to fairly reward creativity?

A Add to the life of the patent, the time it takes for the product to pass through regulatory procedures.

5. How would you modify our regulatory framework that would provide protection for our environment and improve the ability to efficiently conduct biotechnology research.

A The Coordinated Framework for the Regulation of Biotechnology provides a road map for industry. While some may complain that it is complex, the federal regulatory system does provide for the protection of the health and safety for man and the environment. The NIH Recombinant DNA Advisory Guidelines have been adopted by industry and apply to universities. All of these safeguards have not impeded research. But we must allow the system to work.

6. Do you perceive that there is sufficient federal funding directed towards the goal of diversifying our nation's agriculture towards non-food products?

A The USDA still supports traditional commodity crops and invests very little of its resources in diversifying our agriculture into new crops. It also devotes very little of its resources into finding new uses for existing crops. Both of these activities need doing. The Harkin bill is an important step in that direction. Further, it must be viewed as axiomatic that our dependence on non-renewable raw materials cannot last forever.

QUESTIONS FROM SENATOR BOSCHWITZ

1. How important is the private sector for biotechnology research and development?

A The private sector, along with universities, plays an important role in biotechnology research. But in biotechnology development, the creation of new products for society, the private sector is absolutely essential. University research laboratories are designed to make discoveries, not to develop new products for the pharmaceutical, agricultural and other industries. However, it falls appropriately to the private sector to move ideas from the initial discovery to commercial products which benefit mankind.

2. How important is small business for biotechnology research and development?

A Opportunities for entrepreneurship are particularly high in biotechnology. It is far beyond the resources of large companies to develop all the ideas and realize all the potential in biotechnology. For example, a number of independent companies have been created out of technology developed by Monsanto, because even a company of our size cannot begin to do everything it learns how to do given a steady flow of operating capital, it takes only a few talented people to start a firm. Simply put, biotechnology commercialization in the U.S. will involve a great many small businesses.

3. To what extent does present and proposed FIFRA legislation affect biotechnology research and development?

A I see no unique impact on biotechnology under the present FIFRA. The proposed legislation is still evolving and it is thus difficult to gauge the effects on biotechnology. But, uncertainty in the regulatory climate hurts developing technologies. It is essential to protect intellectual property.

4. Would Federal, State and local regulations that increase the risks and costs of biotechnology research and development have an impact on the competitiveness of U.S. business?

A Such regulations would guarantee that America would lose its biotechnology-based businesses to other nations.

5. Please itemize current and proposed legislation that would hamper or reduce the participation of small business in biotechnology research and development with particular emphasis on current and proposed FIFRA legislation. Please include comments or analysis on how agro-[sic] chemical companies may or may not reduce biotechnology efforts should their present chemical based products be made less profitable or should strict and expensive regulation inhibit the development, manufacture and marketing of chemical agricultural products.

A There is no legislation in the U.S. Congress I am aware of for the regulation of biotechnology per se. There have been hearings on the adequacy of current regulation and I understand there may be additional hearings on this subject. As noted above, the current proposed FIFRA legislation is still evolving. We do not need at this time additional legislation or changes in regulation. Further, intellectual property protection must be strengthened through patent term restoration and protection of intellectual property should not be eroded.

This photograph illustrates the value of engineering tomato plants to be resistant to various pests. Caterpillars have attacked the plant on the right but have caused little damage to the plant on the left. There is a small, but important, difference between the two plants. The plant on the left has been genetically altered by the addition of an extra gene -- a protein called Bt. The plant on the right has not been genetically altered.

This photograph illustrates the marker system developed to track genetically engineered bacteria soil. The genetically engineered microorganisms appear blue green in the petri dish. Using the color marker, scientists can track the movement of the released micororganism in the environment.

Daily treatment of pigs with porcine somatotropin for 77 days resulted in a 100 percent increase in loin-eye area and a 70 percent reduction in backfat depth of the pork loin, right, as compared to the untreated loin, left.

from Norcross and Etherton (1986) Penn State Agriculture

This photograph illustrates the impact of porcine somatotropin on the fat content in pork loin. The pork loin on the left is from an untreated hog. In contrast, the pork loin on the right is from a hog treated by porcine somatotropin.

Senator HARKIN. Mr. Harbison, thank you very much for a very fine statement. Before I recognize Dr. Hardy, I did not give an opening statement, but some of the things that you said sort of involved some of the things I was going to say in my opening statement because it deals with agriculture.

As interested as I am in the human aspects, I am also interested in my role on the Agriculture Committee, and representing an agricultural State. Obviously, I am interested in biotechnology as it affects agriculture.

And the one sentence in your statement in which you said that, "My first answer to that is that production is a function of policy, not technology. That within any policy framework technology will obviously reduce costs and obviously benefit the farmer." And that is true, I could not agree with you more.

It seems that our capacity to overproduce is both a blessing and a curse. It is a blessing in that we can obviously feed all our people, and that we do not have hunger. We can feed hungry people around the world. It can be a great part of our foreign policy efforts.

The first thing, of course, with the ability to overproduce more than the demand, prices come down, it causes major disruptions in rural areas, and all of the things that we have seen in the last few years.

It seems that with this capacity to overproduce we have three choices. One, we can continue to do that, with all of the disruption that it causes in rural America, the resulting decline in our workforce in those areas, which I believe inherently, and ultimately, is inefficient for us as a society.

Second, we can leave part of our capacity idle. The third choice is to find some new uses for what we do overproduce, which I believe is the best solution.

It seems we have been locked in the framework of thinking of our policy as producing food and fiber, using that factory out there that we have to produce food and fiber.

To me, biotechnology means that we have a whole new, exciting field out there. With bioengineering we can begin not only to alter plants so that they produce different materials, but to also use the plants that now exist through biotechnology to make new nonfood products.

Products that might replace, perhaps, some of our imported oil, things like that. Obviously, some of that is in the area of Monsanto's concern, in terms of reducing the effect on the environment of use of pesticides and herbicides.

If you can do this through genetic engineering it would reduce the farmer's cost just as much as he does by using things that control pests, but in a more benign manner, as it affects the environment.

One of the problems with full production under traditional methods is that you pollute the ground water and everything else, but if you could have full production through biotechnology and use the products that grow for other than food and fiber, you have the best of all possible worlds.

In that regard, what needs to be done? What kind of long-term policies, long-term programs, need to be done to enable us to go

down this path? I have stated—and I do not know if my figures are correct, but I got these from Senator Glenn—that in the Agricultural Research Service we spend roughly one-half billion plus dollars a year in basic research through all of the different research centers, universities, and everything else.

Something like $6 million of that $500 million is used for finding new plants and new uses of plants. In other words, this new type of research. All the rest of it is used on research on how to produce more.

The bill that I introduced, S. 970, about which the chairman spoke earlier, seeks to change that for a 20-year period of time, to begin shifting that. We would move away from learning just how to produce more to finding out how to bioengineer these new products.

So that within this policy framework farmers can make money, we can have better products, a healthy environment, and all the other things that come along with it.

That was just sort of my opening statement. If you have thoughts on those comments and can further broaden my thinking on it, I would appreciate that. I am not going to cut you off. I am going to call on Dr. Hardy for his statement at this point in time, and again, Dr. Hardy, we welcome you to the committee, and your prepared statement will be made a part of the record in its entirety. I ask you to please proceed as you desire.

[See p. 3 for the prepared statement of Senator Harkin.]

STATEMENT OF DR. RALPH W.F. HARDY, PRESIDENT, BOYCE THOMPSON INSTITUTE, CORNELL UNIVERSITY, ITHACA, NY, AND DEPUTY CHAIRMAN, BIOTECHNICA INTERNATIONAL, INC., CAMBRIDGE, MA

Dr. HARDY. Senator Harkin, I certainly appreciate the opportunity to address this committee on the critical and timely issues you are dealing with with respect to agriculture.

Agriculture clearly has major needs in the United States at this stage. I think they can be reduced to four elements. Clearly, we have got to increase production efficiency. We have got to be the low-cost producer if we are going to be competitive with commodities which most of our agricultural products are in fact.

We, in addition, I think need to create higher value in use foods, higher quality foods, and I think as you have just been saying here, we need to begin to aggressively aim research on nonfood uses so that we can in fact expand the market for agricultural products, so that the supply and balance is again in proper proportion. As well we need to do this in an environmentally neutral way, and I think these are the four elements that agriculture needs.

Biotechnology, in contrast to the things that chemotechnology, in terms of fertilizers and agrichemicals did for us in the 1950's, 1960's, 1970's, and 1980's, and they are still continuing to do to some extent—I think biotechnology is appropriate to these needs. Chemotechnology clearly is not.

Since the two institutions which I represent, the two private institutions are not ones that are probably well known to you, let me make a couple of comments about them.

Boyce Thompson Institute is an endowed institute formed in 1924 to perform science of benefit to agriculture, the environment, and forestry. I think it has had a marvelous track record because its fundamental studies of plant hormones in the 1930's led to the synthesis of 2,4-D, and in fact the first selective herbicide. 2,4-D has sold for more than 40 years at this stage. A $10 million endowment of an institute has led, really, to a $10 billion world sales in 1986 dollars, cumulative, and really led to, in part, the genesis of the herbicide business worldwide, which is now some $8 billion a year.

We are in the process of restructuring that institute to focus on the attractive opportunities that molecular biology now bring. In terms of biological control for pests and diseases, but also, beginning to initiate some work, in clearly this very important area of finding new uses for plant materials.

The other institute which I represent, BioTechnica International, was formed in 1981. One of the major foci of this development-stage biotechnology company is the agricultural area.

We believe we have some of the finest talent that have come from academic institutions into this organization, and have successfully developed a set of what I call tool kits, to introduce into seeds added values.

And so, for example, this alfalfa seed which I show you here will represent the delivery system out of biotechnology, that in the past might have involved a seed, a big fertilizer component, and a big agrichemical component.

So we're going to simplify and condense the delivery system. To this end, we have genetically engineered microbes, microbes called rhizobia that have been applied for some 80 years to our legume crops in this country to increase their nutrient input.

We have genetically engineered rhizobia, that at the greenhouse increased yield of alfalfa by some 15 or so percent, and we have used educational brochures in the community where, next year, we hope to do the first field trials with these genetically engineered entities.

Plant seed clearly will be the big delivery system in plant agriculture, and as you have heard, herbicide resistance, disease resistance, insect, nematode resistance, will probably be the early benefits.

Those will not be the large economic benefits. I think composition change of plants to give them added value in use either as feeds, as foods, or for the nonfood area, will be the key beneficiaries.

Nitrogen fertilization has been mentioned earlier by Dr. Thomas. This is one of the genetic areas where there is a very strong base of scientific information. I would like to indicate that there are five technical hurdles to make self-nitrogen fertilizing crops.

Within the last 4 years, we believe we have been able to cross about 50 percent of those technical hurdles. I think it is not inconceivable, that by the late 1990's, one may in fact have self-nitrogen fertilizing crops beginning to be introduced into commercial use.

Senator HARKIN. By the late 1990's?

Dr. HARDY. By the late 1990's. That is a timing that is extremely different than I used in the early 1980's. I felt that it was some considerable time off.

Now there is still technical hurdles to be crossed, but the rate of progress that we have been making up to this stage gives one some degree of confidence.

Worldwide, nitrogen fertilizer is a $20 billion a year cost, and so, clearly, if we can have self-nitrogen fertilizing crops there will be huge economic benefit.

A huge amount of that nitrogen fertilizer is used in the United States, and therefore, obviously, a huge benefit to the United States.

How is a small company like BioTechnica going to deliver its products to the marketplace? We are in the process of acquiring a seed company, McAllister Seeds, based in Iowa, as our initial delivery system. I thought that might be of some interest to you.

We will also use partnerships with other large companies to deliver some of the benefits of our technology to the farmer.

What is my perception of what we need, then, to strengthen these types of institutions that I have just been talking about?

Clearly, we need people, we need a basic research base that is relevant, we need proprietariness, we need regulation, and we need, as has been mentioned earlier, a favorable investment environment.

In agriculture, it is my perception that we have not been able to attract our fair share of the most creative people, and I think postdoctoral fellowships like the NSF has provided, that represent somewhat higher stipends to attract individuals trained in other fields into agriculture is clearly a major step in the right direction. We need to retrain midcareer people.

Basic research, for the most part, is not done in industry. It is universities, government, and institutes like the one that I am from that perform this activity for the most part. U.S. agriculture has an extremely weak base in basic research versus the health-sciences area. We need, I think, multidisciplinary centers that bring together a multiplicity of skills needed to address the complex basic problems in agriculture.

The new effort by USDA, NSF, and DOE to create a limited amount of money for plant-science centers, $10 million, is a initial step, but a very modest amount of money for the need and for the opportunity.

Senate Bill 970, which you have sponsored, clearly, I think is a significant step in the right direction.

One of the largest opportunities is to create new nonfood uses for agricultural products. I would like to suggest that we need to form a special commission to develop a plan for this opportunity for ag biotechnology. That special commission would represent people outside, as well as within agriculture, to in fact draft the plan as to how to best proceed.

I think it is not inconceivable, that if we brought together scientific capabilities in photosynthesis, solar-energy conversion, if you will, modification of composition of plants, altered microbes to process those plants, that liquid fuels from agricultural products could in fact be a reality.

This is long-term research. It will take longer than traditional agricultural research has to provide a payoff.

PROPRIETARINESS

Clearly, in industry, there needs to be adequate proprietariness to obtain a return. It takes about $1 to $2 million to develop a new corn hybrid up to the marketplace.

It probably will take upwards of $10 million to develop new biotech-generated crops up to the marketplace. Clearly, it is necessary that there be proprietariness to recoup a return on that investment.

REGULATIONS

We need realistic regulations so as not to disadvantage the United States. The recent National Academy of Science report on genetic engineering, which basically said that the process by which you create genetic diversity, whether it is traditional plant breeding, or whether it is by molecular genetic engineering, is not the key. The key is what the product is, and I think that is a major step forward in resolving some of the dilemma that has occurred in this area.

A few weeks ago, Boyce Thompson Institute sponsored a workshop where we brought together a multiplicity of skills from regulatory agencies, industries, and universities—people ranging from molecular biologists to plant breeders, to ecologists to lawyers—to look specifically at genetic engineering in plants, and the technical issues that one needs to consider with their release into the environment for testing, and secondly, their broader commercial use.

I think we made a major step forward in that meeting, because that diverse group of people led to more consensus than I have seen heretofore with respect to the risk.

Looking only at major U.S. crops, and only the near-term changes that we see in those crops, the conclusion was that there was negligible risk for almost all crops, for their introduction for testing as well as for commercial use.

That report we hope to have published in early 1988.

FAVORABLE INVESTMENT ENVIRONMENT

Development stage ag biotechnology companies probably will take at least 10 years before they have products in the marketplace that are of some substance.

We need a favorable investment environment. The health sciences biotechnology development stage companies benefited from R&D limited partnerships to fund some of their more risky research.

Agriculture is somewhat behind them in timing. The R&D limited partnerships do not offer the opportunity to ag biotech development-stage companies that they did to the health sciences area.

Finally, we need international harmonization. We need to make the proprietariness and the regulatory system as harmonious across international boundaries as we can, because with the leading position and strength we have in the United States in this industry, some of the return, a significant amount of the return that we are going to get is from the international arena.

A final comment. We need to have a system to deal with the issues of ag biotechnology as they come up across this country, and

the Boyce Thompson Institute is seeking to put together a National Ag Biotech Council that will involve the University of California through its chancellor, Iowa State through its president, Cornell University through its provost, and the Boyce Thompson Institute—forming a council that will identify the critical issues as they come along in ag biotechnology and provide catalytic support to generate opinions, views, so that consensus can be reached on these issues.

Thank you.

[The prepared statement of Dr. Hardy follows:]

STATEMENT FOR SENATE COMMITTEE ON AGRICULTURE,
NUTRITION, AND FORESTRY

TECHNOLOGY AND LAW SUBCOMMITTEE OF SENATE JUDICIARY COMMITTEE

November 4, 1987

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It is a pleasure to participate in this hearing on Competitiveness in Agriculture. My comments are based from my associations with a development-stage biotechnology company focussed on agriculture and a not-for-profit private institute with a research focus on agriculture, forestry, and the environment.

Let me introduce myself. I am President of the Boyce Thompson Institute for Plant Research at Cornell, the research organization that discovered 2,4-D, the first selective herbicide which, in significant part, led to the development of the agrichemical industry. I am also Deputy Chairman of BioTechnica International, Inc., located in Cambridge, Massachusetts, with affiliates in the U.K. and Canada. This company has developed genetically-engineered N_2-fixing bacteria that enhance alfalfa yields in greenhouse tests and is using biotechnology to create high value-in-use seeds of selected major U.S. crops. In addition, I am a member of the Executive Committee of the National Research Council (NRC) Board on Agriculture, a member of the NRC Commission on Life Sciences and the NRC Board on Basic Biology, and a member of the Board of the Industrial Biotechnology Association. I am also a member of the International Council of Scientific Union's Committee on Genetic Experimentation which addresses international issues of research, training, safety, and others. Prior to 1984 I was associated with the DuPont Company as Director of Life Sciences for Corporate Research and Development.

U.S. agriculture needs help to improve its competitiveness. Biotechnology will be key in improving productivity of crop plants, developing modified and/or new crops and processes for high value-in-use and commodity non-food markets, and enabling agriculture to become

more environmentally neutral in its impact. Biotechnology is relevant to each of the above major future needs of plant agriculture while the old chemotechnology which produced agrichemicals and fertilizers is, for the most part, not relevant.

Biotechnology products and processes for crop agriculture will include diagnostics, microbes, and seeds with the major impact delivered by seeds. Initial seed products are expected to be commercialized in the early 1990s. These seeds will have added value through (1) possession of herbicide resistance enabling better weed control, use of cheaper herbicides, and increased ability to rotate crops; (2) self-protection against diseases and insect pests reducing costs and environmental concerns for synthetic pesticides; and (3) compositional change to give added value to the end use of the crop. It is possible before the end of the 1990s that self-nitrogen fertilizing crops will begin to be used. This opportunity to replace the major economic, fossil energy, distribution and environmental costs of nitrogen fertilizer with a genetically-engineered seed is one of the single largest potential mid-term impacts for biotechnology in agriculture. About half of the laboratory technical hurdles have been achieved for nitrogen-fixing crop plants. In the longer term, genetically-engineered plants should be useful as sources for non-food markets such as chemicals, other materials, and energy. The above products of agricultural biotechnology will enhance not only the international competitiveness of U.S. agriculture but also its domestic competitiveness by decreasing costs and, even more importantly, by expanding uses.

U.S. development-stage and large established agricultural biotechnology companies are leading the world in converting the above potential to reality. What is needed to assure that we continue to lead the world in bringing the benefits of biotechnology for increased economic vitality of U.S. agriculture? The prescription is straight forward. It involves people, basic research, proprietariness, regulation, and favorable investment environment.

People. It is my perception that agriculture does not attract its fair share of the most creative people. The NRC Board on Agriculture has a study in progress on competency needs for agriculture. The nature of U.S. agriculture's current problems and the potential impact of biotechnology necessitates the attraction of highly creative people. Incentives such as graduate and postdoctoral fellowships are needed to bring creative students outside of agriculture into agricultural research and development, and retraining programs are needed to update mid-career researchers and associates to biotechnology.

Basic Research. Basic research is key to generation of new technologies and products and processes. Universities, government laboratories, and private institutes are the main performers of basic research. Established or developing industry performs only modest amounts of basic research. The strength of the base in basic research is key to the high technology industry of biotechnology. U.S. agriculture does not have a strong basic research component as does the U.S. health industry. We need more basic research in agriculture. Many of agriculture's problems need multidisciplinary approaches. The Plant Science Center's Program being initiated by the USDA, NSF and DOE is a positive step, but the $10 million of funding in Year 1 is a very

modest step to meet a major need and opportunity. This program should be expanded aggressively. I have been impressed by the promising interaction between scientists of the Boyce Thompson Institute, Cornell University, and the Agricultural Research Service in generating and formulating quality, interdisciplinary Plant Science Center proposals.

Several high potential agricultural research areas can be identified. One of these is biological control of insect pests and disease as a supplement or alternative to the dominant current use of synthetic chemical pesticides. A 1987 Research Briefing Report on Biological Control in Managed Ecosystems by the NAS/NAE/IOM to the OSTP, NSF, and other government agencies identified the need, direction, and expected reward for expanded research in this area. The products of biological control research will provide expanded opportunities for the agricultural biotechnology industry to develop crops that are protected or protect themselves from disease and insect pests. Several similar areas, in addition to biological control, are high-reward and under-investigated opportunities. A major one is identified below.

The excess crop production capability of U.S. agriculture, coupled with the continuing and successful move of developing countries to self-sufficiency in food, makes it necessary for the U.S. to do research to enable the development of major non-food uses for plants. Herein lies the major new research challenge for U.S. agriculture. We need to bring together some of the most creative minds both within and outside of agriculture to identify these new opportunities. The research should seek improvement that extends from enhanced solar energy conversion to plant compositional changes and to processes to

convert plants to useful products. The proposal by Senator Harkin and others would increase this plant utilization research.

Other countries have been more effective in the past in generating new crops than has U.S. agricultural research. Canada is such an example. Canadians have changed rapeseed to an edible oil crop called canola which is a major source of edible oil in Canada and also a significant Canadian export crop. The crop has been designated GRAS in the U.S.. The U.S. needs to redirect and supplement a significant part of its agricultural research budget to this highest priority area of new uses of plants. The time to pay-off in this research will probably be longer than that to which we are accustomed in agriculture, but the impact in providing new markets for plant agriculture could covert U.S. agriculture from a chronic surplus industry to one in favorable balance with market needs. Biotechnology will be key in this research for product and process development. The regional ARS laboratories established in the 1930s attempted to find new uses for agricultural products but did not have the power of biotechnology to change plants and their processing to products as can be done now. A special commission should be set up to develop a plan for this critical opportunity which will result in new commercial opportunities for agricultural biotechnology companies as well as farmers. This commission should be composed of a broad mix of industry, university, and government leaders with heavy representation outside of agriculture.

Proprietariness. Adequate proprietariness is necessary to encourage risk investment in industrial research to develop biotechnology products. The cost of biotechnology research will exceed

that of traditional plant and animal breeding. For example, it costs about $1-2 million in research and development for each new hybrid corn marketed. The estimated cost for a new corn developed by biotechnology will vary, but an average of $10 million is in the range. Costs for regulatory approval have a major impact on the costs of developing biotechnology products but have little to no impact on traditional products. Obviously there must be higher value-in-use for the biotechnology products, and proprietariness is essential for the biotechnology industry to obtain an adequate return for the value provided and the investment made. Much of the value now provided by agrichemicals, fertilizer and seed is expected to be incorporated into the seed or a seed-microbe combination by biotechnology.

Regulations. Realistic regulations are needed so as to not disadvantage the U.S.'s strong biotechnology position in agriculture. Considerable progress has been made but much remains to be accomplished. The recent NAS report, "Introduction of Recombinant DNA-Engineered Organisms into the Environment: Key Issues," states that biotechnology products are no more inherently risky than those produced by traditional breeding, and the risk benefit in each is solely based on the nature of the product. At a recent workshop meeting organized by the Boyce Thompson Institute and Cornell University, sixty representatives from public-interest groups, governmental regulatory agencies, developing and established biotechnology companies, and universities focused on defining technical issues to be considered for regulating genetically-engineered plants for introduction to each of field testing and commercial use. Disciplines of the participants ranged from ecology to molecular biology to law. A strong consensus

evolved that there were negligible risks to the environment and health-associated areas with introduction of major U.S. crop plants genetically engineered with expected near-term changes such as herbicide resistance, insect and disease resistance, and compositional modifications. The above group focussed only on major crops in the U.S. and recognized that the risks may be different for these or other crops in other parts of the world. Similar meetings as the above are needed to address food issues of genetically-engineered crops and microbes used to improve nutrient input or protect plants against disease, pests, and physical stress.

Regulatory agencies need to adjust their requirements as the assessment of the risk changes based on evaluation of the relevant scientific knowledge. A classification of organisms and types of genetic change should be made to provide guidance for the regulatory agencies. The NRC would be an appropriate organization to perform such a study for plant agriculture, animal agriculture, and environmental clean-up with biotechnology products. Such a study should be initiated immediately so as to provide a representative within one to one-and-a-half years.

Favorable Investment Environment. For three years I have been associated with a development-stage biotechnology company after over twenty years in a large established company. The development-stage company, BioTechnica International, has affiliates in the U.K. and Canada. The established company was DuPont. The development-stage company has attracted outstanding technical talent from universities or equivalent as well as experienced management with an entrepreneurial view from large established companies, developed useful tool kits for

production of biotechnology microbial and plant products and is involved in utilizing those tool kits to develop products that the company expects to market directly or in partnership with large companies. The company expects to be field testing both microbes and crops that are engineered to provide the farmer with significant added value or lower cost.

Adequate financial resource is a key need for development-stage biotechnology companies. There are about ten to fifteen such agricultural biotechnology companies in the U.S.. I view these development-stage biotechnology companies as one of the U.S.'s most valuable biotechnology resources, thereby making U.S. agricultural biotechnology unique from that in other countries. These development-stage companies are using partnerships, such as that recently announced between RJR Nabisco and BioTechnica International, to fund research and development for products that the established company expects to market. Contracts are also used in the same way. However, development-stage companies must obtain financial resources to support research and development for those products they plan to market directly. A favorable investment environment is key to raising these critical resources.

The costs to develop agricultural biotechnology products are somewhat less than for health care therapeutics and the time frame is somewhat shorter. However, the time from initial start-up of an average agricultural biotechnology company to the marketing of its first substantial product will average about ten years. Several health-care biotechnology companies have benefited strongly from use of R & D limited partnerships to finance the cost of research and

development. Tax laws have made R & D partnerships less attractive and thereby have limited use of this route for agricultural biotechnology companies. Development-stage agricultural biotechnology companies are a major source of the U.S.'s agricultural proprietary technology. We need to provide a financial environment that is favorable to the financing of these most valuable resources.

In conclusion, I am convinced that development-stage biotechnology companies can compete in the U.S. and in the world markets. Several have the people and unique research and development capabilities. A few have strong focus and are establishing themselves in the market place. In the near term realistic regulation is a necessity and excessive regulation requirements can severely disadvantage a development-stage company while the impact on an established company would be much less. Furthermore, the benefits of the biotechnology products to the U.S. farmer and society would be unnecessarily delayed by unrealistic regulation, thereby disadvantaging U.S. agriculture. A favorable environment for investment is also key to development-stage companies. In the longer term, adequate proprietariness is essential for the survival of both development-stage and established companies' programs in biotechnology. Harmonization, to any degree possible, of regulation and proprietariness on an international basis will favor competitiveness of U.S. biotechnology companies because of their strong technology positions. "High tech" biotechnology agricultural products will be sold on a world-wide basis. At this time the U.S. is in a world leadership position in biotechnology and should remain so if we attract quality scientists to agricultural research and supplement and redirect our research to the high reward opportunities.

PATRICK J. LEAHY, VERMONT, CHAIRMAN
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United States Senate
COMMITTEE ON
AGRICULTURE, NUTRITION, AND FORESTRY
WASHINGTON, DC 20510-6000

November 23, 1987

Ralph W.F. Hardy
President
Boyce Thompson Institute
Cornell University
Ithaca, New York 14853

Dear Dr. Hardy,

Thank you for participating in the joint hearing on biotechnology held by the Agriculture Committee and the Judiciary Subcommittee on Technology and the Law.

Enclosed are written questions to which members of the Committees would like you to respond. As I mentioned at the conclusion of the hearing, the questions and answers will be included as part of the permanent hearing record.

Please respond to these quesitons by December 14, 1987. If you have any questions, please contact Kathleen Merrigan, Senate Agriculture Committee Staff at (202)224-5207 or Marc Rotenberg, Counsel to the Subcommittee at (202)224-3406.

I appreciate your assistance in compiling a complete record on the issues before the Committees.

Sincerely,

Patrick J. Leahy

PATRICK J. LEAHY
Chairman

QUESTIONS FROM COMMITTEE MEMBERS
FOR DR. RALPH HARDY

NOVEMBER 4, 1987 HEARING ON BIOTECHNOLOGY

Questions from Senator Leahy

1. We have the world's premier biomedical research system, anchored by the National Institutes of Health. Should we have a similar national institute dedicated to agricultural research or biotechnology in general?

2. How can we ensure that we have adequate human resources to transform the promise of new biotechnologies into economic growth?

   a. What steps need to be taken to provide the necessary training and retraining of employees in biotech industries?

   b. Should we do more to encourage engineers in manufacturing and product delivery, as opposed to basic research?

   c. Should we encourage the training of American students abroad in countries such as Japan?

3. What do we have to fear from the release of biotech products into our environment? How serious is the threat? What measures should we take to protect our environment?

4. Are there areas of biotechnology that we should decide right now not to pursue? What are the dangers if we do pursue developments in these areas?

5. What role do small firms play in biotechnology innovation? How do we ensure their survival in the biotech craze? Are people right to worry that in 10 years there will be only 4 or 5 giant firms controlling biotechnology in this country?

6. How do we involve the general public in the biotechnology decision-making process in a meaningful way?

7. Do you agree with the National Academy of Sciences finding that we need to infuse our basic research with $500 million annually? If this figure is unrealistic, what figure would you suggest and where should we direct our support?

8. The Europeans and Japanese have undertaken many cooperative efforts and joint research programs such as EMBO,

EUREKA, and BRAIN. What comparable programs can or should be developed in the United States?

9. Will biotechnology promote the loss of biodiversity, as we develop highly specialized crops and animals? What can we do to lesson the risks?

10. Do you think it is possible to reach an international agreement on research safety guidelines for biotechnology? Would such an agreement be enforceable? How should we begin the process?

Questions from Senator Conrad

1. What are the key reasons that new research ideas are not developed into marketable products? In your response, please include your thoughts on whether it is difficult to find investors and members of the financial sector willing to finance this development, and whether companies are hesitant to invest long-term capital and resources into the development and refinement of new research products? What kind of governmental financial assistance would be helpful to companies and individuals trying to commercialize new biotechnological products?

2. In the 1970s, the U.S. was the leader in basic research on semiconductors. Today, we are struggling to keep up with the semiconductor manufacturing capabilities of Japan. How can we prevent a similar decline in our current lead in the biotechnology field?

3. Would it be useful to set up a council which would act as a liaison between private and public researchers, and the academic, industrial, the financial sector, and marketing sector? Such a council would help these sectors explore and develop the potential for producing new products.

4. If the federal government should take a role in helping compainies through the developmental stage of product commercialization companies and projects and assure that any available federal funds are directed at the most promising areas of agricultural biotechnology?

5. Biotechnica has affiliates in both Canada and the United Kingdom. Does this affiliation with foreign companies flow, at least in part, from a need to avoid burdensome regulation in this country? What problems or impediments has your company found in the regulatory process?

Questions from Senator Karnes

1. Do you feel that the United States is on the leading edge of this technology?

2. What do you consider to be the most productive area of biotechnology up to this point?

3. Where do you see biotechnology taking us in the next ten years in terms of tangible benefits?

4. What do you feel we can learn from other high technology areas which are undergoing rapid development?

Questions from Senator Harkin

1. What types of support do other countries provide to their business concerns in support of bringing new research based products on line? What are other countries doing that you believe the U.S. should adopt to better provide financial resources for their research companies in the area of biotechnology?

2. We cannot reasonably expect any profit making company to take basic research results and try to make use of it in a direction that is highly risky and where the results will not be known for 10 or 15 years. Given that reality, where should the government's role stop and the private company's role begin?

3. What are the barriers to university-company cooperation in biotechnology research that you believe should be modified?

4. If you were the sole decider of what should be done in the area of patents, how would you change the present system as it applies to biotechnological products so as to fairly reward creativity?

5. How would you modify our regulatory framework that would provide protection for our environment and improve the ability to efficiently conduct biotechnology research.

6. Do you perceive that there is sufficient federal funding directed towards the goal of diversifying our nation's agriculture towards non-food products?

Questions from Senator Boschwitz

1. How important is the private sector for biotechnology research and development?

2. How important is small business for biotechnology research and development?

3. To what extent does present and proposed FIFRA legislation affect biotechnology research and development?

4. Would Federal, State and local regulations that increase the risks and costs of biotechnology research and development have an impact on the competitiveness of U.S. business?

5. Please itemize current and proposed legislation that would hamper or reduce the participation of small business in biotechnology research and development with particular emphasis on current and proposed FIFRA legislation. Please include comments or analysis on how agrochemical companies may or may not reduce biotechnology efforts should their present chemical based products be made less profitable or should strict and expensive regulation inhibit the development, manufacture and marketing of chemical agricultural products.

Boyce Thompson Institute for Plant Research
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Ralph W.F. Hardy

December 11, 1987

Senator Patrick J. Leahy
Chairman
Committee on Agriculture, Nutrition, and Forestry
U.S. Senate
Washington, DC 25010-6000

Dear Senator Leahy:

The following are my responses to the questions submitted in your letter of November 23, 1987.

Questions from Senator Leahy

1. No, I do not favor creating a new Institute but would favor a new major division of NSF whose function would be to support new directions in research for agriculture. I would favor a new major division in the USDA if it could be established so as not to be in direct competition for funding with the essential USDA research for ongoing directions.

2. Agriculture has a record of not obtaining its fair share of the best talent based on a recent report by the NRC Board on Agriculture. We need to provide postdoctoral support at higher than normal rates to attract outstanding scientists trained outside agriculture to agriculture. We need also to provide funds to universities for the retraining/updating of mid-career scientists in industries, especially maturing ones such as agrichemicals, and also mid-career scientists in government laboratories.

   As biotechnology products enter the market place, the expected need for marketing and sales personnel will grow rapidly as well as modest growth in research personnel. Agricultural engineering departments should expand their activities to include agricultural bioengineering.

   Yes, we should encourage American students to train abroad in countries such as Japan so that they can provide leadership in guiding American biotechnology products for the Japanese market. The cultural experience may be at least as important as the technical experience.

3. The threat from the release of biotechnology products into the environment is minimal. A recent workshop meeting at the Boyce Thompson Institute which focussed on genetically-engineered crops and their field testing and commercial use--and involved regulators, biological scientists and environmental scientists--led to a high degree of consensus that the risk was minimal for most major crops in the U.S. We should categorize risks and assign Institutional Biosafety Committees, or their equivalents, responsibility for approving limited field trials and only require EPA or USDA approval for the significant risk categories. Some additional guidance needs to be provided for IBCs or their equivalents so there would be uniformity among them. The National Research Council could be asked to provide a document in which there would be guidance on categorization of risks for biological material and test areas. The current review process at the federal level is excessive for the vast majority of releases that are minimal risk and as a result substantially slows research progress and greatly expands cost.

4. Yes, there are areas that we probably should not pursue at this time. An example would be the incorporation into plants of genes for substances with significant toxicity to humans. As experience expands, some areas precluded at this time might become acceptable. This process was a key to the original and modified NIH-RAC Guidelines.

5. Small firms play the major role in biotechnology innovation. This has been true in the health care area and appears to be true in the agricultural area with the exception of one or two major firms. We need to create an environment favorable to investment in these firms so as to provide the needed resources for research and product development. Possibly a federal guarantee such as has been used for mortgages would provide the comfort to encourage investors to provide loans or equivalent to small biotechnology companies. The small development-stage agricultural biotechnology companies are one of the major competitive advantages that the U.S. has in agricultural biotechnology at this time.

   I doubt that there will only be four or five grant firms controlling biotechnology in the U.S. in ten years. Such a concentration is expected in a mature industry such as agrichemicals at this time, but I would not expect it in biotechnology for 25 to 40 years; and the breadth of industries impacted by biotechnology may make such concentration even more remote.

6. We need to teach the facts of biotechnology in our K-12 school system and thereby communicate by this established route with the broader public. Benefits of the products of biotechnology will also influence the public's perception.

7. I agree with the general sum of $500 million annually. I chaired an earlier NRC report in 1985 on Biosciences for Agriculture with a similar recommendation. It should be reached in a step-wise fashion. Agricultural research has been inadequately financed for the last several decades, and agriculture has major needs. New non-food uses for plants must be found. Research is the key to developing such uses. In addition, research is needed to improve productivity and add value to food crops. The commitment of additional funds will attract scientists outside agriculture to agriculture.

8. The proposed NSF/DOE/USDA plant science center funding and the NSF science and technology centers, as well as the Harkin Bill, will provide funding for cooperative research efforts. These initiatives are excellent and can bring together a necessary mix of skills to solve complex agricultural problems such as, e.g., biological control of pests.

9. Biotechnology can be both negative and positive for biodiversity with, in my view, the potential for an overall favorable impact on biodiversity.

10. Organizations such as COGENE of ICSU played a useful international role in the early days of the safety of rDNA laboratory research. Perhaps such technically-based international organizations could be useful to move toward uniformity.

Questions from Senator Conrad

1. Transfer of technology to products has a poor record in the U.S. My experience as Director of Life Sciences in DuPont sensitized me to the difficulty of this process in a large company. My experience as President of BioTechnica International suggests that the transfer is somewhat less difficult but not easy even in a development-stage company. The key, in my judgement, is the right people and the financial resources to support the activity. As stated above, federal guarantees to investors could be key in this area. However, people are also key. The U.S. is much more effective in training creative scientists who do research than it is in training creative scientists or other professionals who transfer technology to new products.

2. Provide a favorable investment environment for development-stage biotechnology companies and do not overburden biotechnology with an excessive and slow-moving regulatory process.

3. I do not see a major advantage of a council. The incentive for success and the desire to succeed in development-stage companies will drive the establishment of relationships without a council. Leading private and public researchers are in continuous contact by phone, visits, and on a periodic basis at scientific meetings.

4. I favor investors making the decision on support and the federal government providing the climate to encourage such investment. The above is the case for products for markets that are economically attractive. For markets that are inadequately attractive for private initiative than direct, government support may be necessary.

5. The BioTechnica affiliates were founded to provide complimentary technology, access to research outside the U.S., access to additional products and foreign markets, and as an investment. Avoidance of burdensome regulation was never a basis. BioTechnica's request to EPA to field test genetically-engineered Rhizobia under TSCA has been a learning experience for BioTechnica and presumably also EPA since it was the first TSCA submittal to BioTechnica and, I assume, also to EPA. It has also been costly but we trust that each of our learning from this process will greatly simplify similar future applications.

Questions from Senator Karnes

1. The U.S. is the world leader in both health care and agricultural biotechnology.

2. Health care biotechnology has been most productive to date. I expect improved microbes and seeds to become of major importance in the 1990s.

3. Biotechnology will improve crop productivity and provide value-added foods. In the 10-15 year period it could provide major new non-food uses for crops if we initiate major research initiatives for this opportunity.

4. Development-stage companies have been very important to the computer industry. The same will probably be true in biotechnology. However, each technology has its unique character and we should not seek to broadly apply other experiences to biotechnology.

Questions from Senator Harkin

1. I believe that we should develop support systems that are consistent with the nature of U.S. biotechnology companies and not apply support systems that, for example, are used in Japan where the role of large corporations is great. We need a federal support system that is consistent with a favorable investment climate for development-stage companies.

2. Basic research to generate new information has and should be performed with, for the most part, public funds at university and government laboratories. The private company should perform applied research to convert the results of basic research to potential profits. For example, research to develop major new non-food uses of plants is primarily the responsibility of government. Research to convert a known biocontrol agent to a useful product is the domain of industry.

3. Various experiments are being performed in university-company cooperations. Some will work and be duplicated; some will work and not be repeated. People interactions will be the key to successful cooperation. It might help to have some scientists who work in both industry and universities. Another approach is to have industrial and academic exchanges.

4. I would provide patent protection for all non-human organisms--animals, plants, microbes--where an invention has occurred. I would also allow the filing of patents up to one year after publication in both foreign as well as is now possible in the U.S. I would have international uniformity for patenting. I would be very cautious in granting extremely broad-process claims.

5. I would simplify, categorize risks, and decentralize so that only the above average risks would be considered at the USDA and/or EPA for research activities in the field. More centralized regulation is appropriate for commercial use as opposed to field testing.

6. No. This is a major opportunity and needs a national plan and substantial funding. Your Bill is a step in the right direction.

Questions from Senator Boschwitz

1. Private sector is key for product and process development. Public sector is key for basic research.

2. Small business is responsible, to a major extent, for the current competitive advantage of U.S. agricultural biotechnology.

3. Slows field research. See above comments on decentralization. Proposed environmental biosafety committees are a step in this direction, but institutional and environmental biosafety committees should become one so that additional committees are not unnecessarily created. A document is needed to provide guidance for uniformity. The RAC has approved such guidance for greenhouse and laboratory animal experimentation facilities.

4. Such excessive regulation would increase costs, slow progress, and substantially decrease competitiveness.

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5. It is of utmost importance that current and proposed legislation does not increase the cost or the time for approval when the risk is minimal as it appears to be for many agricultural biotechnology products. It also would be desirable to utilize the food and drug administration's priority-approval approach where the product seeking approval appears to have fewer environmental impacts than does an existing product or it meets a need that is un-met.

In most cases agrichemical companies are part of broad-based chemical companies, and I would not expect--based on my several years in a major chemical company--for such companies to reduce their biotechnology effort if their present products were made less profitable by realistic legislation. Slow and excessive regulatory requirements for biotechnology products over an extended period would have far greater effect in reducing their biotechnology effort.

Sincerely yours,

Ralph W. F. Hardy

Ralph W. F. Hardy (gc)

RWFH:gc

Senator HARKIN. Thank you very much, Dr. Hardy. Our distinguished chairman is back. I first of all want to thank you very much. I think we have received some great testimony and something to build on here.

I sort of gave a small speech and asked a question involved in that, and now I have to leave. I know that Mr. Harbison had some thoughts on the question I had asked dealing with agricultural biotechnology.

I am sorry I have to leave. I would like to correspond with you on that issue, and perhaps I could stop out and see you in St. Louis one day.

The CHAIRMAN. That, incidentally, is well worth it. I have done that, as Mr. Harbison knows. In fact we first met out there, and it is worthwhile. I would be delighted to see members of the committee go out.

It was made very obvious to me, your research plants are that open to us, and I think that is very important.

In this particular committee you will find people who are most interested in that, and you may regret the hospitality, but I intend to encourage Senators from both parties to keep going out there.

Mr. HARBISON. You are welcome.

The CHAIRMAN. Thank you.

Senator HARKIN. I just had one question, that if you would answer for the record after I am gone. You talked, Dr. Hardy, about a special commission setup to investigate some of these possibilities.

Mr. Harbison, you talked about a special panel. I would like to know if you are both talking about the same thing, or, are these different aspects of it. I did not quite understand that. OK. Thank you very much. I am sorry. Thank you, Mr. Chairman.

The CHAIRMAN. Thank you. In fact I think we will continue with the question Senator Harkin asked——

Senator HARKIN. Excuse me just a minute. That is the new porkchop. That is the old one.

Mr. HARBISON. That is the lean one.

The CHAIRMAN. All right. I missed breakfast. I will probably miss lunch. You are making me hungry already. We can go to Senator Harkin's question, but I notice in both Mr. Harbison's prepared testimony, where you said on page 14 at the top: "Let me suggest that you pull together a panel of large and small company executives who can help you find out what is needed."

And then also, in Dr. Hardy's prepared testimony, on page 6, you say: "A special commission should be set up to develop a plan for this critical opportunity which will result in new commercial opportunities for agricultural biotechnology companies as well as farmers. This commission should be composed of a broad mix of industry, university, and Government leaders, with heavy representation outside of agriculture."

How about all three of you discussing this further. Let's start with Dr. Thomas. Dr. Thomas, how do you feel about what Mr. Harbison and Dr. Hardy have said here?

Dr. THOMAS. Specifically, about the need for a commission to take a look at what is needed in the way of science, and applications of science to the long term? Is that what you have in mind?

The CHAIRMAN. Yes.

Dr. THOMAS. I would agree. I would think also, that if we still had in existence PSAC, the President's Science Advisory Committee, working as it did during the 1960's and early 1970's until it was killed off, they would long since have launched panels and standing bodies to consider this very important matter.

But I would agree that there is a need for a new collection of brains, and brainpower to take a look at this.

Mr. HARBISON. We may be addressing a different aspect. We may have hold of the same elephant here but we have got a different part of it.

I was addressing, or trying to address, Senator, a more defined issue, a narrower issue of, what do you need to keep—particularly small companies, but also large ones as well—in business dedicated to the eventual production of products, which is the ultimate test of the technology. It is all interesting, but if you do not produce something at the end of it, it has just been interesting. How do we keep them in business over a protracted period of time?

Dr. Hardy has suggested it is 10 years from inception to success of the business. I suspect that is very true. Companies like ours have literally put in hundreds of millions of dollars funded from other businesses to allow the development to go on.

Now a company, an entrepreneurial company that has one idea and is going down the road toward one product does not have $100 million to throw in the pot. What do they need to become successful and remain in business, and what did the large ones even need to be sure we are around 10 years from now developing the product?

That was the focus of my remarks. I find nothing wrong with the other idea, but mine was not that all-encompassing, and I thought your committee should have the benefit of a grouping of people—scientists and executives from large and small companies who could probably, in the composite, lay out for you what we need to be here a decade from now, before we worry precisely about some of the other technologies. That was the genesis of my remarks.

The CHAIRMAN. Dr. Hardy.

Dr. HARDY. Right. I agree that we addressed two different, but I think equally critical, aspects.

One relates to the commercialization process, and what is the climate to create for the current commercialization process. The other activity relates to a major new, in my view, necessary research focus to find other uses for agricultural products which are now in surplus, and in my view are going to be in surplus for years to come.

The rest of the world has started in the 1950's, the developing countries, to go from inadequacy to self-sufficiency, and India has made marvelous progress.

China, clearly, under its new system is making progress. One might expect the U.S.S.R. to make significant progress. So there is not going to be a need for U.S. agricultural produce, significantly, for the rest of the world.

What do we do with this major production capability that we have, and I think we have got to look at generating research for new uses. That we, on on the industrial side, in 2000 and beyond,

will be very excited about that base of science because it will give us a new set of commercial opportunities.

But I think we have got to get started today down that road. We tried, in a little institute I am involved with, the Boyce Thompson Institute, in terms of identifying where should we start in plant utilization research, and it is a problem, I think, too large for any single entity to do significant new things.

I do not think agriculture alone can chart this course because I think it will tend to regenerate directions that we may have taken in the past, and that is why I would recommend we have a broad commission of highly creative individuals from a cross-section that would say here is a plan of how we can generate new uses for agricultural products.

I think energy can be one of these, but it is going to take major research in the photosynthesis area to improve solar energy conversion that is less than 1 percent from the Sun's energy to what we get in dry matter in plants, major compositional changes, and major process changes.

There are a whole array of others that I think could be identified. Also, it will expand the base of support for agriculture research, I think, if we have a broad commission as opposed to one that is just within agriculture. Agriculture clearly needs to expand its base.

The CHAIRMAN. I tend to agree with you, especially on that. Incidentally, Senator Harkin had left a question here and I just wonder if any of you know the answer to this.

The question is: How does Federal funding for agriculture biotech research compare with funding for biomedical biotech research? Do any of you know, offhand?

Dr. THOMAS. I do not know what the figure is for basic science and agricultural research, but I am sure that it is very much less than what is going into biomedical science.

Dr. HARDY. I was at a meeting on Monday of this week where NIH indicated it was putting about $2 billion a year into biotechnology research. The whole of governmental research for agriculture is about $2 billion, and in my view, hugely on the more applied and the support for the now businesses as opposed to the future.

I would guess 10 percent of medical biotechnology research for ag biotechnology may be on the optimistic side.

The CHAIRMAN. Thank you. Just as I was leaving to go to the meeting over at the Capitol, I had raised what some use for shorthand, the "Frankenstein factor."

Are there areas of biotechnology we should decide not to pursue, and decide right now not to pursue?

Why don't we just go right down the line. Dr. Thomas, how about you, sir?

Dr. THOMAS. I am, as I mentioned in my prepared testimony, optimistic, and really, I find it hard to imagine scenarios that strike me as dangerous to the world or to the environment.

I think I would just as soon not see efforts made to alter the human genome by technological means. On the other hand, I can imagine no objection to the use of biomedical technology to alter somatic cells in order to try to reverse disease within the individ-

ual, but I do not want to change the human germ line. It seems to me that it needs another 50 or 100,000 years to run in its present irresponsible fashion, and I do not want to touch it.

I do not have any anxieties about crazy scientists——

The CHAIRMAN. There are some who think that same basic irresponsibility may make the whole question moot.

Dr. THOMAS. I think there is a role for Government agencies, heaven knows, to keep an eye on what is going on, both in industrial and university laboratories, but it does not seem to me very scary. Nobody is going to decide that two heads are really better than one, and use genetic engineering for that.

The bacterial world, which has been here since 3.7 billion years ago, has been occupied and using most of its energy for recombinant DNA and the exchange of genetic information. There is now a respectable theory, that all the bacteria on the Earth, comprising by far more, in dry weight, than any other form of life on the Earth, that all of those bacteria which look to us so widely different are really products of the same original clone, and they have been exchanging—as we know they do—DNA and RNA across their own cell borders, as one of the ways they make their living.

We could not possibly do anything new, I do not think. The diphtheria bacillus produces diphtheria toxin, and therefore is able to produce diphtheria as a disease, not because of its own genes, but because it has caught a virus. It has got a bacteriophage that gets into it in nature, and those strains of the diphtheria bacillus that have got bacteriophage in their genome make toxin under instructions from the phage.

The same thing is true for streptococci that carry certain toxins that produce scarlet fever. It is a commonplace observation. It has been going on for hundreds of millions of years, and I do not think we are going to invent anything novel when we engage in the kind of genetic engineering that is going on now.

On balance, then, I am optimistic, Senator, and I do not think this is a risky business.

The CHAIRMAN. Mr. Harbison, do you think there is anything we should be putting off limits right now?

Mr. HARBISON. I find it extremely difficult to follow those erudite comments and add to them.

The CHAIRMAN. Except your company must sort of have to debate that question periodically, do you not?

Mr. HARBISON. That is not the issue if you believe you can do something about it, and chose to do, which frankly never crosses our minds to do, so it is a "paper tiger," in the sense that we would attempt to do some of the things that are theoretically drawn out and possible over a long period of time.

So, to us, it does not present an issue. I have never met anyone along Dr. Thomas' view, who suggested they thought it was a good idea, they were working on it, they were going to work on it.

I suppose it is all theoretically possible, but one is dealing with an issue I guess of exceedingly long-term ethics, and I do not know that I have a great answer for that, unless one wants to tackle the esoteric job of the ethics of human manipulation, if one knew how to do it. It simply is not a real issue to us, Mr. Chairman.

The CHAIRMAN. Dr. Hardy.

Dr. HARDY. Let me restrict my comments to the agricultural area. The things that we will develop in the agricultural area will need tender loving care for their survival in the environment, not any different than the current crops that we have need tender loving care for them to survive.

So it is an artificial as opposed to a natural environment that we create, that allows their survival. As a result, there is little in the area of agricultural innovations that gives me concern.

I think we do need some more guidance than we have at this stage, and I know at the moment, the National Research Council Board in basic biology is seeking funding to bring together scientists to classify what the risks might be from different types of changes.

And I think for regulatory agencies, for industries, for universities, for the public, such guidance would be a useful thing for us to have in place, and could facilitate this industry.

The CHAIRMAN. What happens if we come in second in an international biotech race? Mr. Harbison, would you please respond to that question?

Mr. HARBISON. Sure. Well, semiconductors may be a good example to start with if you want to be second, and there was the case of where we had the technology, and, for a variety of reasons, the production mechanisms and capabilities went to Japan, and in a short period of under a decade, we went from having better than 50 percent of the world markets down to wherever we are at the moment. I guess it is in the high 30's, or something, and dropping, as far as I know, and will continue to drop, in my humble judgment.

So it is not an imagined phenomenon that this could happen even though you are first in research. That simply is not so. Number two, let me take the Japanese, but there are certainly others in the business, and some issues of this were addressed in your hearings this morning.

The Japanese are particularly good in the application of technology to practical products. The manufacturing, the reduction of the ideas to manufacturing. Now why is that?

Well, in part it is because of the structure of their industry. Their attention to that, their devotion of substantial sums of money to it. They particularly happen to fit biotechnology I think more so than other areas, because they have for a long time been excellent in fermentation and probably ahead of the United States, over a period of years, in purification and sterilization systems.

So they kind of fit this category. Now, if you go back, it is all part of the same "warp and woof," Mr. Chairman. The small companies, such as we have been discussing today in particular, have to get from a concept to a product. Otherwise it is just fun.

And to get to a product they have to make it, and to be able to make it they have to be able to ferment it and purify it, and do all these things, and they have to put money into it.

The financial markets in the United States have very short tempers with that. So the net result is these companies must, one way or another, find funding either from American sources or from foreign sources.

When they find it from foreign sources, very often, the quid pro quo is the exchange of technology. That is how come they give them the money. They do not give it because they like them.

So this is going on constantly. Now what we have to do, I believe, is to get in the hands of these companies some reasonable mechanism and capability of being able to go from their research stage to a production stage of the product, or it is over.

And the Japanese, the way they organize, with the whole MITI complex, the sharing of very low interest rates, the division of technology responsibilities, the protection of the home market so no one else can produce or sell the products within the home market—all of that labyrinthine system builds companies that eventually can be put into world markets as healthy companies. They come over and compete with our companies where we have no market protection. I am not going down the protectionist route, that is not what I am after, but we have got to get some——

The CHAIRMAN. But there is a big difference between setting up protectionist legislation and setting up a system whereby we can encourage—as you mentioned—those small companies, or, make it possible for large companies to enter into joint enterprises, or other things that make American ventures not only competitive at home but also competitive abroad.

Our Nation has shown ability for innovation, but sometimes not the ability then to market that innovation, at least in a world where transportation means you can go anywhere in the world in a matter of hours, and communications, you go there in microseconds.

Sometimes, a difficulty we have here is trying to get across to people that helping our companies is a lot different thing than just putting up protectionist legislation, saying that we will protect a dying industry, or saying we will not allow anybody to compete with us.

Mr. HARBISON. Sure. We have the opportunity here. We are on the front end of the industry, not on the rear end, trying to resurrect it, or pump life into it as it is dying. We are up front in this one. I think back to my suggestion earlier to you. I think to bring these companies in we have to understand, the committee should understand, what do they face, what are their problems, what sort of things do they need to keep ongoing in this competitive world which is where they operate? I do not know all the answers.

The CHAIRMAN. I look at just the world-trade balance. We have got the Russians who are working on engineering frost-resistant wheat. African countries may conceivably develop drought-resistance crops.

Do we lose markets for agricultural products there, or do we develop them ourselves? I do not know the answers to all of these questions. Many of our Senators have additional questions, and I would like to be able to submit some questions in writing to the three of you, if I can. If you get too many of them and it looks burdensome, please let me know and we will try to cut them back down.

We have some other material for the hearing and I will keep the record open for a couple of weeks.

This is just the first of what is going to be a series of hearings of this nature, because it is an area, one, that we do not know enough about in the Congress, and two, it is an area where industry, Government, and academia, are trying to sort out where the answers are. Many individuals have some very good ideas, and I would like to use the Judiciary Committee and the Agriculture Committee as a repository of at least some of those answers.

[Whereupon, at 12:05 p.m., the committee adjourned, subject to the call of the Chair.]

[Material submitted for inclusion in the record follows:]

8 THE WALL STREET JOURNAL WEDNESDAY, NOVEMBER 4, 1987

Genentech Inc. Receives Broad Patent For Basic Gene-Splicing Techniques

By MARILYN CHASE
Staff Reporter of THE WALL STREET JOURNAL

Genentech Inc. won a broad patent covering the basic techniques by which the biotechnology industry turns colonies of microorganisms into factories for the manufacture of useful products.

The patent could mean that the company will get future royalty payments from the sale of many products produced and marketed by its competitors.

Robert A. Swanson, founder and chief executive officer of the South San Francisco, Calif.-based company, hailed the patent as "recognition of Genentech's pioneering scientific efforts." He said Genentech won't use the patent to block other companies from creating new products, and indicated Genentech will offer nonexclusive licenses to other biotechnology companies "at reasonable rates."

The patent doesn't contain anything revolutionary to the biotechnology industry; its claims were filed in 1979, said Thomas Kiley, Genentech's vice president for corporate development. The patent covers fundamental know-how for transplanting foreign genes for the production of proteins and hormones into microbial hosts. Colonies of these hosts—such as yeast and bacteria—are then raised in fermentation tanks where they churn out proteins such as insulin and human growth hormone.

But the nature of the patent may mean most major biotechnology contenders will need to get a license from Genentech to continue playing in the field.

One competitor, Chiron Corp., Emeryville, Calif., is generally prepared to comply, said Edward Penhoet, president. Though Chiron hadn't seen the details of the patent, Mr. Penhoet indicated his company is prepared to comply. "My view is that we have to be pro-patent," he said. "Aggressive patenting is good for the biotechnology industry. And if Genentech deserves a patent, they deserve to be paid for it."

Cetus Corp. also in Emeryville, declined to comment. A spokeswoman said the company's officers hadn't seen the patent.

"We've been waiting for this for a long time," said M. Kathleen Behrens, an analyst with Robertson, Colman & Stephens in San Francisco. "It's been rumored for about a year that Genentech would receive an 'industry-encompassing' patent, and this sounds like it."

Co-Inventors Named

Genentech issued its news release after the close of trading yesterday. Its stock closed in national over-the-counter trading at $35.25 a share, down $2.

Named as co-inventors are Drs. Keichi Itakura and Arthur Riggs of the City of Hope, a Los Angeles research institution. Drs. Itakura and Riggs carried out their work under Genentech sponsorship.

The patent, which has already been issued in 20 other countries, is the industrial counterpart of the landmark Cohen-Boyer patent, issued to Stanley Cohen of Stanford University and Genentech co-founder Herbert Boyer of the University of California. That patent dealt with splicing genes from one organism to another; the Riggs-Itakura patent deals with using gene-splicing to create whole factories of hybrid microbes, Genentech's Mr. Kiley said.

The new patent doesn't deal with specific products, but broadly describes classes of products which encompass most of the fruits of the young biotechnology industry.

"It's very, very important with regard to biotechnology research," Ms. Behrens said. "It sounds like, from here forward, everyone who conducts research will need to get licensed." Financially, she added, "it could be very consequential if people comply. It's a question of how Genentech chooses to implement protection."

Royalty Rate

Genentech's Mr. Kiley said the company hasn't yet decided on what royalty rate it will charge. However, the customary royalty rate for nonexclusive licenses of this kind are from 0.5% to 1% of sales, noted Ms. Behrens. "If you ask for more, you run the risk that a company, or a group of companies, will stand up to you," she added.

"We don't intend to use the patent to extract immodest or ruinous royalties," Mr. Kiley said, adding the company planned to make licensing decisions on a case-by-case basis, and might employ a sliding scale for flexibility.

How aggressively Genentech will defend its patent remains to be seen. The company made it clear yesterday it would prefer others make the first move. "For the time being," Mr. Kiley said, "we're going to let each individual company make its own judgment as to whether its activities require a license under the patent. Plainly, if companies make incorrect judgments, the time may come when we have to help them get it right."

Another major question that will govern the patent's impact is whether the claims extend beyond yeast and bacteria, to embrace newer biotechnology "factories" comprised of mammalian cell cultures. Many of the newer products of biotechnology—including Genentech's clot-dissolving drug TPA—are produced in cultures of mammal cells. On its face, the patent doesn't address mammalian cell cultures.

George B. Rathmann, chairman and chief executive officer of Amgen Inc., Thousand Oaks, Calif., said Amgen will consider getting a license but cautioned the patent's sweep is wide open to interpretation. "If interpreted most narrowly, there are certain bacterial (production) systems that wouldn't even be covered. If interpreted most broadly, it could cover all production systems in bacteria, yeast and mammalian cells."

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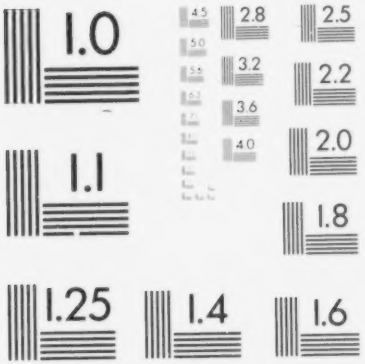

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